



## The Impact of Physical Fitness Activities on Enhancing Immune System Function and Disease Prevention Capabilities

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**SUMMARY:** *In particular, diseases occur in relation to immune function, and proper exercise is necessary to improve immunity. In this research, controlled experiments, mathematics, and statistics, as well as questionnaires, will be used to determine how physical fitness exercises relate to immune system function and disease occurrence. Firstly, a controlled experiment was conducted to determine the effects of physical fitness exercises on the immune system function. Secondly, correlation analysis was done to prove the relationship between the immune system function and physical fitness factors. Lastly, the correlation between physical fitness exercises and disease occurrence were determined based on exercise frequency, intensity, and duration. It was found that physical fitness exercises improved the immune system function and helped to maintain good health and reduce diseases. Exercise frequency, intensity, and duration have an effect on disease occurrence.*

**KEYWORDS:** *Controlled experimental method; Mathematical statistics; Immune system function; Physical fitness exercise*

### 1 Introduction

In recent years, because of the advancement of the economy and medical science and technology, humans obtain more comprehensive medical resources for dealing with disease, improving human safety and extending human lifespan. Combined with the reduction of birth rate, the process of the aging population is becoming faster, which will bring great influence to the economy, politics, and society of China and pose great pressure on social welfare, elderly welfare, and healthcare [1]. With the arrival of the aging era, the health problems of old people have been becoming a new topic of public concern and the eternal quest of life science researchers. Some recent researches find that one reason for lowering the quality of life of middle-aged and old people is aging-related immune dysfunction. It will make them more vulnerable to the invasion of various pathogens and more susceptible to tumor, infection, and autoimmune diseases [2-5]. In 1969, American pathologist Wolford put forward the immunological theory of aging and coined the term "immunosenescence," suggesting that the immune system plays an essential role in the process of aging [6].

Over the past decade, the relationship between immune function and physical exercise has garnered increasing attention. It is widely recognized that regular physical activity can enhance immune function, boost the activity of phagocytes and natural killer cells, and prevent infectious diseases [12]. With growing emphasis on health and exercise, exercise immunology has rapidly advanced, with numerous experimental studies validating and exploring the interplay between physical activity and immunity.

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In the last ten years, the link between the body's immune response and exercise has become more prominent. It has been well documented that regular physical activity improves immune response and activates phagocytic and natural killer cells, thereby preventing diseases [12]. The rising importance of exercise in health promotion has led to the quick development of exercise immunology, and several experiments have been conducted in this regard. For instance, Nieman, D [13] first proposed the "open window theory" of exercise and immunity, suggesting that high-intensity strenuous exercise induces lymphocyte apoptosis, leading to a temporary decline in immune function. This is analogous to opening a window in the body's immune system, making it easier for various bacteria and viruses to invade and increasing susceptibility. Consequently, a widely accepted view holds that appropriate exercise intensity and volume can enhance immune function and resistance to infection. However, excessive, high-intensity, and exhausting exercise that causes significant bodily damage will result in pronounced immune suppression [14-17].

Natural killer cells are lymphocytes which can perform immune activities on their own inside the body. Aerobic exercises are helpful in increasing the proliferative activity and immunity of NK cells [18-20]. But, the proliferative ability of NK cells reduces with increasing age. Idorn, M & Hojman, P [21] observed that physical exercise increases the entry of NK cells in the blood stream. Exercises are considered an important factor in the treatment of cancer. Exercising acts as an adjuvant to treat cancer as it recruits and allows infiltration of NK cells into solid tumors. Moderate intensity exercises were seen to increase NK cell proliferation and immunity [22]. Thus, physical exercise provides a drug free method of improving body's immune system. In a pilot study done by Toffoli, E et al. [23], participants with cancer undergoing chemotherapy were randomly assigned to either exercise group (n=8) or control group (n=6). The study demonstrated that exercise interventions (moderate-to-high intensity resistance and aerobic training) maintained NK cell activity by preserving degranulation levels and increasing expression of activation receptors. Pal, A et al. [24] observed that short-term intense exercise increases IDO (indoleamine 2,3-dioxygenase) levels while decreasing KIR2DL1 (Killer Immunoglobulin-like Receptor 2DL1) expression; while long-term aerobic exercise reduces IDO levels and increases NKG2D (Natural Killer Group 2 D-like) expression. These findings indicate that sustained moderate exercise enhances NK cell activity, thereby indirectly boosting the body's disease resistance.

Several myokines caused due to contraction as well as non-muscle cytokines generated during exercise have been identified to be involved in immune metabolism, but it is believed that such an issue has never been addressed experimentally in the context of exercise physiology. However, both IL-6 and IL-10 levels rise after exercising and stimulate anti-inflammatory macrophage function through pathways causing better oxidative metabolism [25, 26]. Findings by Otaka, N et al. [27] indicate that myosin, an endurance exercise-induced myokine, suppresses macrophage inflammation by inhibiting protein kinase B, a regulator of cellular metabolism. Thus, exercise may also enhance immune function by modulating muscle-secreted factors. Padilha, C et al. [28] proposed that exercise influences energy substrate availability via  $\beta$ 2-adrenergic signaling and upregulates anti-inflammatory cytokines, particularly emphasizing the importance of appropriate aerobic exercise for immune modulation and immune cell homeostasis. Moreover, several exercise-induced proteins regulate immune metabolism. For example, elevation in growth differentiation factor-15 during exercise improves oxidative metabolism of macrophages [29].

Nutrient receptors are equally important in controlling immune metabolism; hence there is great potential for exercise to impact the metabolic programming of immune cells by influencing the availability of nutrients or directly affecting these intracellular signaling proteins [30, 31]. Activation of AMP-activated protein kinase (AMPK) occurs under low

energy conditions and is triggered by exercise in muscle and other tissues [32]. In the immune system, AMPK has been used to inhibit inflammation in macrophages, dendritic cells, and T cells [33]. Inhibition of T cell metabolism by AMPK occurs via regulation of a glucose-dependent metabolic checkpoint for maintaining T cell bioenergetics and viability, both essential functions for the development and anti-pathogenic properties of T cells [34]. The activation of AMPK in macrophages also promotes fatty acid oxidation. Exercise can affect immune metabolism through autophagy by interacting with AMPK and Sestrin proteins in skeletal muscle [35].

New research has also highlighted the importance of specific intermediates in modulating the immune system. Interestingly, glycolysis and tricarboxylic acid (TCA) cycle metabolites, like lactate and succinate, have demonstrated their abilities in modulating the activities of various immune cell populations [36, 37]. It is well-known that exercise results in the production of more succinate and lactate [38]. Hence, their higher amounts could be linked to the modulation of immune system functions. Furthermore, recent studies conducted by Zhang, H et al. [39] have indicated that exercise is responsible for inducing trained immunity in Kupffer cells through the process of metabolic rewiring. As per the mechanism of action, exercise-induced HMGB1 facilitates itaconic acid metabolism while depending upon NRF2 signaling pathway for influencing the functioning of Kupffer cells.

This research aims at finding the association between physical fitness exercise, the efficiency of the immune system, and the capability to prevent diseases. In order to determine the impact of physical fitness exercise on the efficiency of the immune system, an experiment involving 60 students from the Faculty of Sports Rehabilitation at University B was conducted. Thereafter, a quantitative analysis was performed to find the connection between the efficiency of the immune system and the capability to prevent diseases among 400 students at their sophomore year at University B. Lastly, a questionnaire was distributed among 421 people living in City A.

## **2 The Impact of Sports and Fitness Activities**

### **2.1 Enhancing the Immune Function of the Respiratory System**

Breathing is essential for human life. Regarding the function of breathing, physical exercise takes on a special importance, which involves maximally raising the ability of oxygen uptake of the body. Numerous researches proved the efficiency of the development of the breathing function through exercising in terms of increasing coordination between respiration and movements [40]. In general, the breathing system requires constant activity. People participating actively in physical training have less variance in the values of certain parameters than the people who do not participate in sports activities. Moreover, their muscles of breathing are more developed, their ventilatory capacity is higher than that of an average person. The breathing vital capacity grows significantly; there is also increased respiratory difference, and thus there is improvement of breathing functions. People constantly participating in physical exercises also have bigger oxygen debt capacity, higher resistance to hypoxia, higher oxygen intake and consumption rates, better adaptation to breathing rhythm and breathing technique.

### **2.2 Enhancing the Immune Function of the Human Circulatory System**

The human circulatory system is extremely intricate, made up of thousands of veins, arteries, and capillaries within the body. It provides the blood supply that transports food and oxygen to various organs and limbs. In addition to its functions, it establishes a strong network for the

immune response, supplying immune cells to organs wherever and whenever necessary to neutralize any unwanted chemicals produced by the body itself or from the outside world. The circulatory system is an essential element of the immune system, providing pathways for immune defenders to move around all parts of the body. When bone marrow does not work efficiently, fat and clots block arteries and veins, thereby hindering or postponing the process of production and transportation of these defensive agents. This makes the body lose in the war against foreign substances within the human immune system. On the other hand, when the circulatory system receives enough nutrients and arteries and veins are free of obstructions, blood moves freely, thus giving the body more chances of winning this battle. Physical activities benefit the circulatory system in several ways. They open up many capillaries, reduce blood lipid content, and increase the immune cell count.

### **2.3 Enhancing the Regulatory Functions of the Human Nervous System**

The regulation of the immune response is one of the most important functions performed by the nervous system. There are two methods through which the nervous system affects the immune system, including psychologically and physiologically. On a physiological level, the nervous system acts as an important channel of communication between the brain and the immune system. Emotions play a very important role on a psychological level. Research indicates that those who are pessimists visit the doctor's office many times more often than optimists and have a higher chance of developing diseases. Being pessimistic could affect the immune response negatively. However, optimists usually have better immune responses than pessimists. Physical exercise promotes healthy functioning of the central nervous system by making the brain neurons more excitable and flexible. It maintains equilibrium throughout the body, resulting in increased performance and adaptive responses.

### **2.4 Methods for Non-Specific Immunity in the Human Body**

There are many factors affecting the immune system of human beings. Among all these factors, only suitable physical exercises can improve the activity of the immune system. Physical exercises act as stimulants that initiate an adaptive response from the immune system, thereby stimulating the immune system of the body. The immune system contains a highly efficient recognition system that perceives any change in the internal environment of the body through exercises, thus initiating various activities of the immune system. It includes an increase in the number of sensitized lymphocytes and antibody production. In addition, physical exercises provide adequate stimulation to the body's immune system, which maintains a high level of activity.

From the above discussion, it is concluded that regular physical exercises help in improving immune functions. Moreover, suitable physical exercises increase the number of immune cells at rest. Hence, regular physical exercises increase the immunity of the body against diseases. [41].

## **3 Study Population and Methods**

### **3.1 Control Experiment Method**

#### **(1) Experimental Subjects**

For this experiment, 60 undergraduate students from the Department of Sports Rehabilitation at University B were chosen as subjects. Criteria for choosing subjects include:

- 1) The subjects should not be physical education majors.

2) They should be in perfect health condition.

3) It should be voluntary participation.

(2) Experimental Grouping

The selected 60 undergraduates were randomly grouped as either the fitness group (experimental group) or reference group.

(3) Pre-experimental Assessment

Before conducting the experiment, all subjects were tested for their immune functions. Capillary blood samples were collected through fingerstick into anticoagulant tubes, followed by extraction of plasma and detection using human IL-1, IL-6, IgG, and IgM kit via enzyme-linked immunosorbent assay (ELISA). Reference ranges of the aforementioned four parameters (as specified by the reagents manufacturer) are as follows:

Human Interleukin-6 (IL-6): 7.16–47.3 ng/L.

Human Interleukin-1 (IL-1): 42.8–293.6 ng/L.

Human Immunoglobulin G (IgG): 28.5–187.1 µg/ml.

Human Immunoglobulin M (IgM): 4.27–29.4 µg/ml.

(4) Training Protocol

The training cycle spans 12 weeks.

1) Experimental Group

Aerobic exercises are conducted on Monday and Friday evenings from 6:30–8:00 PM and Wednesday mornings from 10:00–11:30 AM.

First, the warm-up phase included 10–15 minutes of low-to-moderate intensity basic step routines (primarily aerobics and Latin aerobics) and stretching exercises accompanied by music. After a 2–3 minute rest, participants engaged in fundamental training such as running, jumping rope, basketball, and badminton.

2) Control Group

The control group maintains their normal lifestyle and habits without specialized exercise training.

(5) Experimental Requirements

1) Before the experiment begins, communicate with participants to encourage their understanding of the experiment's significance and physical benefits. Emphasize the importance of controlling exercise intensity. Assistants supporting the experiment should be instructed to promptly remind participants to maintain exercise intensity and duration.

2) Post-experiment assessment: Testers measured relevant indicators for subjects in both the experimental and control groups. After completing data entry, pre- and post-test data for both groups underwent statistical analysis using SPSS tests to determine significant correlations. Results were analyzed and discussed to draw conclusions.

## 3.2 Mathematical Statistics Methods

(1) Experimental Subjects

Second-year students from University B were selected as research subjects.

(2) Experimental Process

As per the testing procedures and standards specified by National Student Physical Fitness Standards (2014 version), there were eight standard tests carried out, including stature, body mass index, breathing volume, standing long jump, running test (50 meters), sit and reach test, pull-ups (males) /sit-ups for 1 minute (females), and run test (1000 meters for males/800 meters for females). The physical fitness was graded into four categories: Excellent ( $\geq 90.0$  points), Good (80.0–89.9 points), Passing (60.0–79.9 points), and Failing ( $< 60.0$  points). The data were acquired from the database on physical fitness of the university. 100 students were randomly selected from each category and took immune system tests as described above.

The raw data were sorted using Excel 2013, while SPSS 24.0 software was used for statistical analysis. Pearson's correlation analysis was adopted to determine the correlation between physical fitness levels and immunity factors [42] with significance level set as 0.05.

### 3.3 Questionnaire Survey Method

#### (1) Study Population

Citizens over 18 years old in City A.

#### (2) Questionnaire Design

The survey form is divided into three parts. The first part contains questions related to the demographic data of the respondents, the second part relates to their health status, and the third part involves their participation in physical exercises. After finishing the development of the survey form and testing its reliability and validity, it was distributed to citizens over 18 years old in City A randomly. 500 forms were distributed, out of which 450 were collected, with 421 being valid surveys, which equals 84.2% effectiveness.

## 4 Results and Analysis

### 4.1 Analysis of the Effects of Physical Fitness Activities on Immune System Function

Based on the 3.1 design of the controlled experimental method, this chapter will investigate the effects of physical fitness activities on immune system function.

#### 4.1.1 Changes in Immunity Indicators Before the Experiment

Prior to the experiment, a homogeneity of variance test was conducted using SPSS 26.0 on the overall immune indicators of the experimental and control groups. The test results are shown in Figure 1. The mean values for interleukin-1 (IL-1), interleukin-6 (IL-6), immunoglobulin G (IgG), and immunoglobulin M (IgM) in the experimental group were 134.05 ng/L, 25.63 ng/L, 78.63 ng/L, and 15.31 ng/L, respectively. The mean values for the four indicators in the control group were 133.96 ng/L, 25.21 ng/L, 78.44 ng/L, and 14.96 ng/L, respectively. No significant differences were observed in the mean values of the four immune indicators ( $P > 0.05$ ). This indicates that there were no significant differences in immune status between the two groups of students prior to the experiment, making them suitable for subsequent comparative studies.

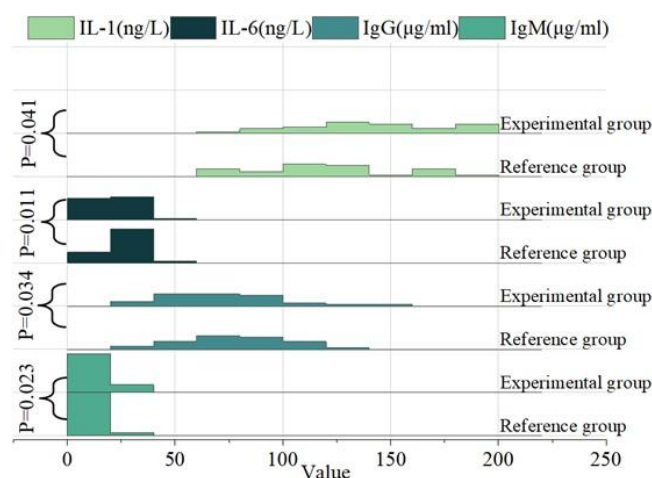


Figure 1: The pretest of the immune system was tested for variance

### 4.1.2 Changes in Immunity Indicators After the Experiment

Following the experiment, SPSS 26.0 was again employed to conduct a homogeneity of variance test on the overall immune indicators of the experimental and control groups. The test results are presented in Figure 2. The mean values for interleukin-1 (IL-1), interleukin-6 (IL-6), immunoglobulin G (IgG), and immunoglobulin M (IgM) in the experimental group were 173.63 ng/L, 41.63 ng/L, 126.63 IgM, and 18.93 IgM, respectively. The mean values for the four indicators in the control group were 137.52 ng/L, 25.77 ng/L, 79.63 IgM, and 14.52 IgM, respectively. Significant differences were observed for IL-1 and IL-6 ( $P < 0.05$ ), while highly significant differences were noted for IgM and IgG ( $P < 0.01$ ). This indicates that the experimental group exhibited significant changes in immune function following physical fitness training.

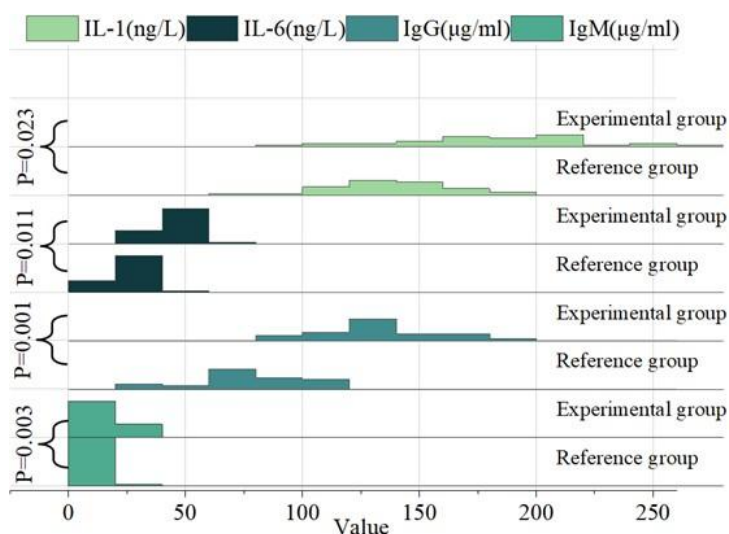


Figure 2: The posttest of the immune system was tested for variance

Based on the above experimental results, it was concluded that after the experiment, subjects in the experimental group showed significant increases in IL-1 and IL-6, and very significant increases in IgM and IgG. Physical fitness exercises exert a certain promotional effect on the secretion and synthesis of interleukins and immunoglobulins in the human body, demonstrating significant improvements in the immune function of the subjects. The greater increase in IgG levels may be attributed to the enhanced synthesis of immunoglobulins facilitated by the increase in fat-free mass. Furthermore, relevant studies confirm that IgM is frequently used for diagnosing infectious diseases. The substantial changes in IgM levels following exercise further substantiate the improvement in immune function among the subjects due to physical fitness activities.

## 4.2 Correlation Analysis Between the Immune System and Physical Health

Based on the mathematical statistical methods designed in Section 3.2, this chapter analyzes the correlation between the immune system and physical health.

### 4.2.1 Analysis Results for Male Samples

The statistical correlation between male physical health levels and immune system indicators is shown in Figure 3. When male physical health levels are rated as excellent, good, or qualified, they exhibit a positive correlation with overall immune system levels. Conversely, when physical health is rated as unqualified, it shows a negative correlation with overall immune

system levels. This indicates that as the immune system strengthens, male physical health levels also improve accordingly.

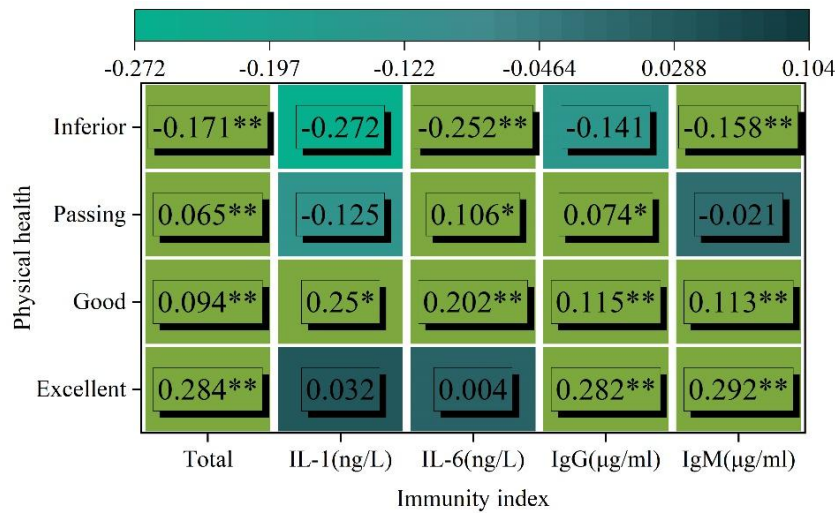


Figure 3: Sample analysis of male

#### 4.2.2 Analysis Results for Female Samples

The statistical correlation between women's physical health levels and immune system indicators is shown in Figure 4. When women's physical health levels are rated as excellent or good, they exhibit a positive correlation with overall immune system levels. On the other hand, when classified as good or poor, there is a negative correlation with general immune system levels. This also strengthens the argument that improvement in immune system performance corresponds to an increase in physical health levels. In addition, compared to males, females have higher physical health needs for proper immune system performance.

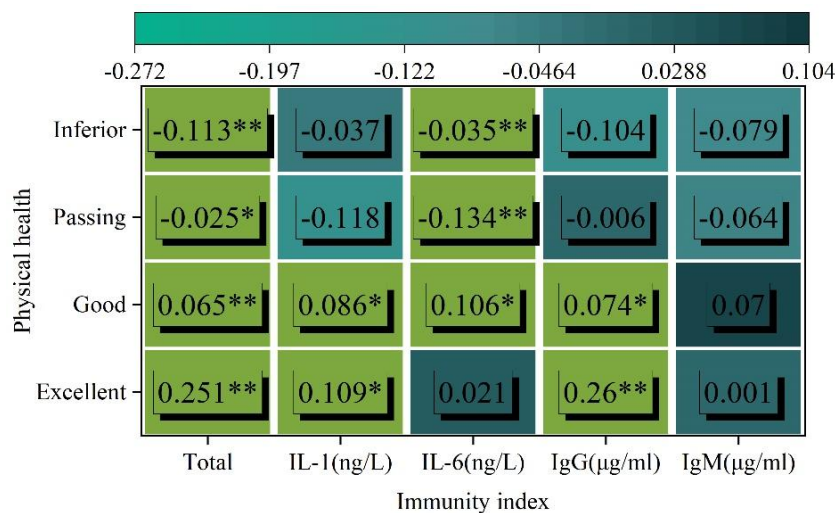


Figure 4: Sample analysis of female

In summary, the immune system is closely linked to overall health. To enhance immune function, it is essential to improve physical well-being, thereby enabling effective disease prevention.

### 4.3 Analysis of the Relationship Between Physical Fitness Activities and Disease Prevalence

To sum up, the immune system has close associations with good health. For improving the functioning of the immune system, it is important to promote the good state of physical health, and thereby achieve good preventive effects.

According to the questionnaire survey method stated in Section 3.3, the relationships between exercise regularity, exercise time, exercise intensity, exercise persistence and disease prevalence will be analyzed in this chapter.

Table 1 shows the statistics about disease prevalence within our research sample group. Among the total 421 samples, 237 cases are diseased, covering 8 kinds of diseases. The disease with the largest prevalence is COPD (25.74%).

*Table 1: The prevalence of the survey was counted*

Type of disease	Male	Female	Proportion (%)
Ischaemic Heart Disease	11	13	10.13
Stroke	12	12	10.13
COPD	30	31	25.74
Diabetes Mellitus	12	14	10.97
Allergic Rhinitis	14	16	12.66
Cancer	12	11	9.7
Chronic Kidney Disease	15	10	10.55
Depression	11	13	10.13

#### 4.3.1 Correlation Between Exercise Frequency and Disease Prevalence

To investigate the connection between exercise frequency and disease prevalence, this study statistically analyzed disease prevalence among people with varying exercise frequencies through questionnaires. One-way ANOVA was used to test for differences using exercise frequency as the independent variable, as illustrated in Figure 5. From the findings, it can be observed that the one-way ANOVA for disease prevalence among the surveyed population, where exercise frequency is the independent variable, yielded a P-value of  $0.028 < 0.05$ , meaning there is a significant difference. It indicates the presence of a connection between the frequency of exercises performed by the residents and disease prevalence. Statistical analysis of disease prevalence among the surveyed populations with varying exercise frequencies shows that having an exercise frequency of 3-4 times a week or 5-6 times a week can minimize disease prevalence.

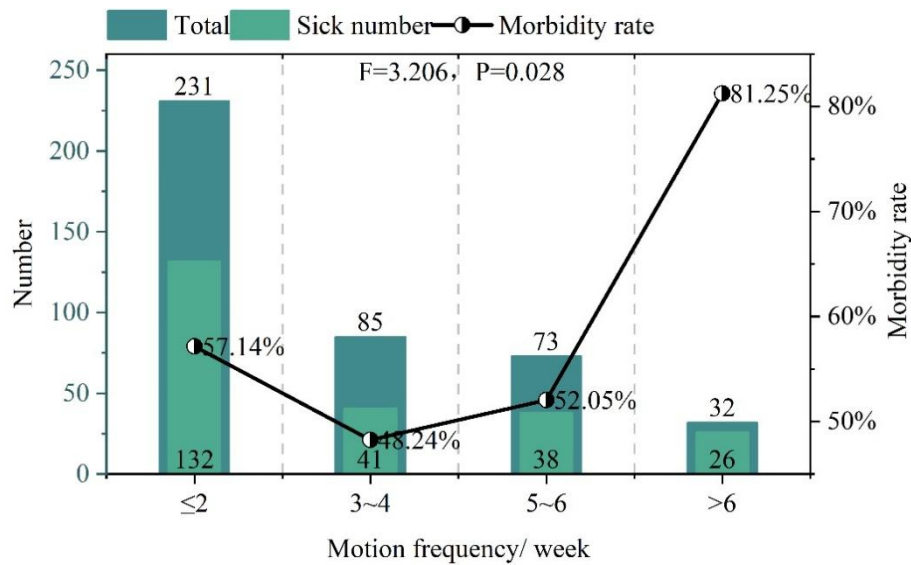


Figure 5: Analysis of single factor variance of motion frequency

#### 4.3.2 Correlation Between Exercise Duration and Disease Prevalence

One-way ANOVA of disease prevalence depending on the exercise duration is represented in Figure 6 below. It was found from the test that the disease prevalence among the respondents depends significantly on the duration of exercise ( $P=0.017 < 0.05$ ). This means that when the duration of exercise falls within the interval of 31-90 minutes, there will be a low disease prevalence.

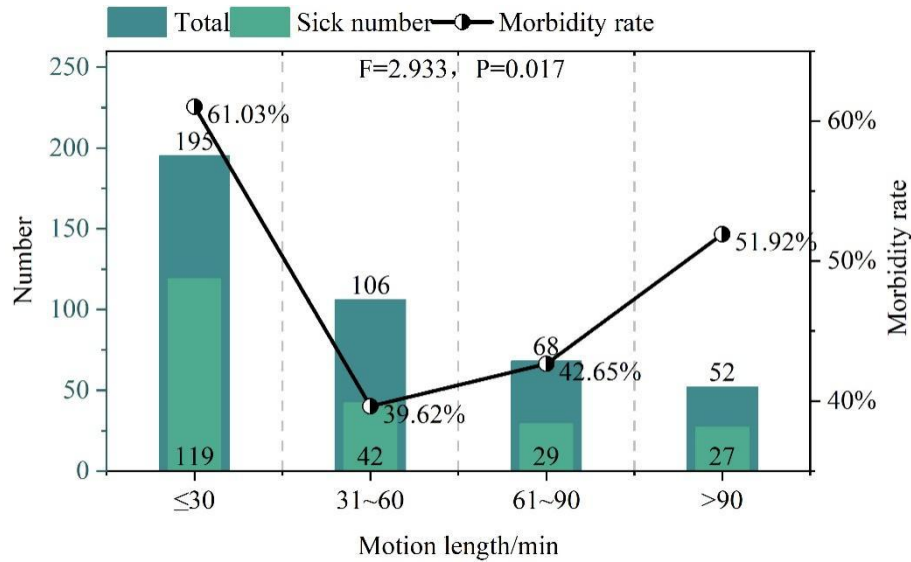


Figure 6: Analysis of single factor variance of motion length

#### 4.3.3 Correlation Between Exercise Intensity and Disease Prevalence

The use of RPE scale for assessing the intensity level of exercise activity is done through questionnaire survey. The relationship between the results from the RPE scale and exercise intensity is presented in Table 2 below. Exercise intensities were grouped into four categories: low, moderate, high, and very high intensity.

Table 2: Conversion relational

Sensory fatigue	Motor intensity	The maximum heart rate percentage (%)
Easy (0-4)	Low strength	40-60
Slightly tired (5-6)	Medium strength	61-70
Tired (7-8)	High degree	71-85
Very tired (9-10)	High intensity	≥85

After translating the perception level of fatigue into the respective exercise intensity, a one-way ANOVA was performed where the exercise intensity was the factor used for examining the disease prevalence. The outcome of this analysis is presented in Figure 7 below. From the figure, it can be noted that the value of the P-test conducted for examining the disease prevalence among the population under study using the factor of exercise intensity yielded 0.013. Again, the value is less than 0.05, thus implying that the exercise intensity significantly influences the disease prevalence within the studied population. Additionally, from the data analysis in Figure 7, it was clear that individuals with the lowest disease prevalence exercised at "moderate intensity."

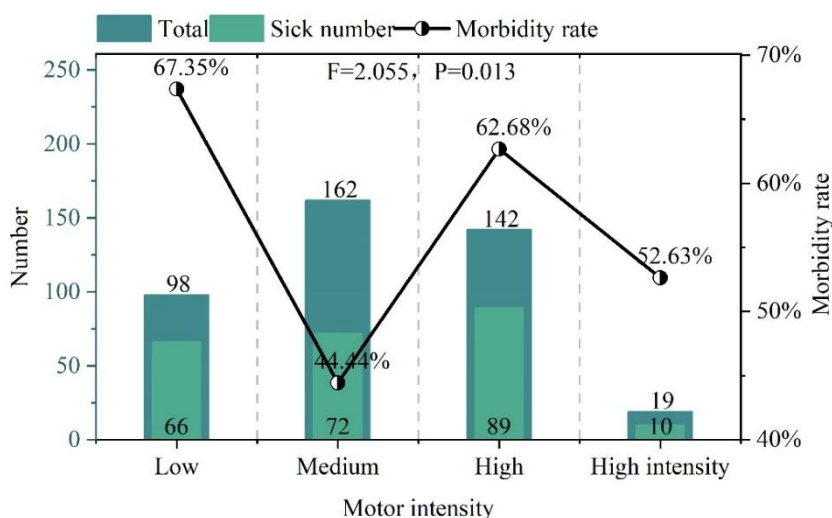


Figure 7: The analysis of the single factor variance analysis of motion intensity

#### 4.3.4 Correlation Between Exercise Duration and Disease Prevalence

Exercise adherence time is a critical variable in determining the individual exercise behavior and an important determinant in disease incidence. The responses of the survey are presented in Figure 8 below. The analysis of variance (ANOVA) conducted for disease incidence in the surveyed population using the exercise time as a factor gives a P-value of  $0.001 < 0.01$ , which shows a highly significant difference. Hence, there is a highly significant effect of exercise time on disease incidence in the population. Statistics show that increased exercise time results in reduced disease incidence; people who adhered to exercise for more than 12 months had 17.2% lower disease incidence than those who adhered to exercise for three months or less.

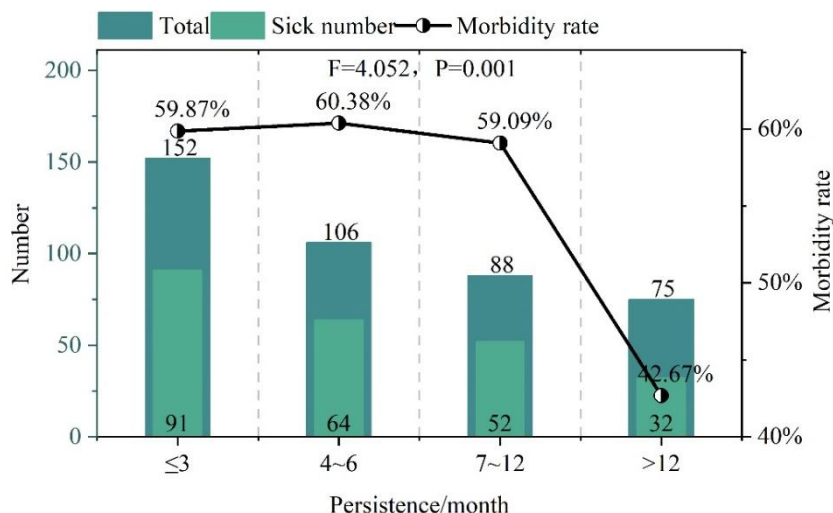


Figure 8: The analysis results of the single factor variance of persistence

To conclude, generally speaking, there exists a specific relationship between residents' physical exercise and disease prevalence.

## 5 Conclusion

Controlled experiments, mathematical statistics, and questionnaires were used in this research to test the impact of physical exercises on strengthening human immunity and disease-preventing ability. They have confirmed the following results:

(1) Physical exercise can strengthen human immune function. Interleukin level increases significantly ( $P < 0.05$ ) after sustaining regular exercising habit, and immunoglobulin level rises greatly ( $P < 0.01$ ).

(2) There is a link between immune function and general health condition, and women need a better health condition than men in order to attain a healthy immune system.

(3) Exercise behavior shows a specific relationship with disease prevalence. Sustained exercise behavior is linked to fewer diseases. Exercise 3–6 times every week for 30 to 90 minutes links with low disease prevalence.

## References

- [1] Aw, D., Silva, A. B., & Palmer, D. B. (2007). Immunosenescence: emerging challenges for an ageing population. *Immunology*, 120(4), 435-446.
- [2] Yung, R. L. (2000). Changes in immune function with age. *Rheumatic disease clinics of North America*, 26(3), 455-473.
- [3] Valiathan, R., Ashman, M., & Asthana, D. (2016). Effects of ageing on the immune system: infants to elderly. *Scandinavian journal of immunology*, 83(4), 255-266.
- [4] Fuentes, E., Fuentes, M., Alarcón, M., & Palomo, I. (2017). Immune system dysfunction in the elderly. *Anais da Academia Brasileira de Ciências*, 89(1), 285-299.
- [5] Aspinall, R., & Lang, P. O. (2018). Interventions to restore appropriate immune function in the elderly. *Immunity & Ageing*, 15(1), 5.

- [6] Goyani, P., Christodoulou, R., & Vassiliou, E. (2024). Immunosenescence: aging and immune system decline. *Vaccines*, 12(12), 1314.
- [7] Pawelec, G. (2018). Age and immunity: what is “immunosenescence”? *Experimental gerontology*, 105, 4-9.
- [8] Liu, Z., Liang, Q., Ren, Y., Guo, C., Ge, X., Wang, L., ... & Han, X. (2023). Immunosenescence: molecular mechanisms and diseases. *Signal transduction and targeted therapy*, 8(1), 200.
- [9] Lian, J., Yue, Y., Yu, W., & Zhang, Y. (2020). Immunosenescence: a key player in cancer development. *Journal of hematology & oncology*, 13(1), 151.
- [10] Fülöp, T., Dupuis, G., Witkowski, J. M., & Larbi, A. (2016). The role of immunosenescence in the development of age-related diseases. *Revista de investigacion clinica*, 68(2), 84-91.
- [11] Ponnappan, S., & Ponnappan, U. (2011). Aging and immune function: molecular mechanisms to interventions. *Antioxidants & redox signaling*, 14(8).
- [12] Forte, P., Branquinho, L., & Ferraz, R. (2022). The relationships between physical activity, exercise, and sport on the immune system. *International Journal of Environmental Research and Public Health*, 19(11), 6777.
- [13] Nieman, D. C. (1994). Exercise, infection, and immunity. *International journal of sports medicine*, 15(S 3), S131-S141.
- [14] Chamorro-Viña, C., Fernandez-del-Valle, M., & Tacón, A. M. (2013). Excessive exercise and immunity: the J-shaped curve. In *The active female: health issues throughout the lifespan* (pp. 357-372). New York, NY: Springer New York.
- [15] O’Keefe, E. L., Torres-Acosta, N., O’Keefe, J. H., & Lavie, C. J. (2020). Training for longevity: the reverse J-curve for exercise. *Missouri medicine*, 117(4), 355.
- [16] López, P., Chamorro-Viña, C., Gómez-García, M., & Fernandez-del-Valle, M. (2023). Exercise and immunity: beliefs and facts. In *The active female: Health issues throughout the lifespan* (pp. 503-526). Cham: Springer International Publishing.
- [17] Simpson, R. J., Campbell, J. P., Gleeson, M., Krüger, K., Nieman, D. C., Pyne, D. B., ... & Walsh, N. P. (2020). Can exercise affect immune function to increase susceptibility to infection?. *Exercise immunology review*, 26, 8-22.
- [18] Lin, M. L., Hsu, C. C., Fu, T. C., Lin, Y. T., Huang, Y. C., & Wang, J. S. (2022). Exercise training improves mitochondrial bioenergetics of natural killer cells. *Medicine & Science in Sports & Exercise*, 54(5), 751-760.
- [19] Zimmer, P., Bloch, W., Schenk, A., Zopf, E. M., Hildebrandt, U., Streckmann, F., ... & Baumann, F. (2015). Exercise-induced natural killer cell activation is driven by epigenetic modifications. *International journal of sports medicine*, 36(06), 510-515.
- [20] Llaveró, F., Alejo, L. B., Fiuza-Luces, C., López Soto, A., Valenzuela, P. L., Castillo-

- García, A., ... & Lucia, A. (2021). Exercise training effects on natural killer cells: a preliminary proteomics and systems biology approach. *Exercise immunology review*, 27.
- [21] Idorn, M., & Hojman, P. (2016). Exercise-dependent regulation of NK cells in cancer protection. *Trends in molecular medicine*, 22(7), 565-577.
- [22] Pan, H., Meng, R., Jia, Z., Zhang, J., Ma, W., Liu, Y., ... & Li, Q. (2024). Exercise: a non-drug strategy of NK cell activation. *Brazilian Journal of Medical and Biological Research*, 57, e14144.
- [23] Toffoli, E. C., Sweegers, M. G., Bontkes, H. J., Altenburg, T. M., Verheul, H. M., van der Vliet, H. J., ... & Buffart, L. M. (2021). Effects of physical exercise on natural killer cell activity during (neo) adjuvant chemotherapy: a randomized pilot study. *Physiological reports*, 9(11), e14919.
- [24] Pal, A., Schneider, J., Schlüter, K., Steindorf, K., Wiskemann, J., Rosenberger, F., & Zimmer, P. (2021). Different endurance exercises modulate NK cell cytotoxic and inhibiting receptors. *European journal of applied physiology*, 121(12), 3379-3387.
- [25] Park, M. J., Lee, S. H., Lee, S. H., Lee, E. J., Kim, E. K., Choi, J. Y., & Cho, M. L. (2015). IL-1 Receptor Blockade Alleviates Graft-versus-Host Disease through Downregulation of an Interleukin-1 $\beta$ -Dependent Glycolytic Pathway in Th17 Cells. *Mediators of inflammation*, 2015(1), 631384.
- [26] Ip, W. E., Hoshi, N., Shouval, D. S., Snapper, S., & Medzhitov, R. (2017). Anti-inflammatory effect of IL-10 mediated by metabolic reprogramming of macrophages. *Science*, 356(6337), 513-519.
- [27] Otaka, N., Shibata, R., Ohashi, K., Uemura, Y., Kambara, T., Enomoto, T., ... & Ouchi, N. (2018). Myonectin is an exercise-induced myokine that protects the heart from ischemia-reperfusion injury. *Circulation research*, 123(12), 1326-1338.
- [28] Padilha, C. S., Von Ah Morano, A. E., Krüger, K., Rosa-Neto, J. C., & Lira, F. S. (2022). The growing field of immunometabolism and exercise: Key findings in the last 5 years. *Journal of Cellular Physiology*, 237(11), 4001-4020.
- [29] Rosa-Neto, J. C., Lira, F. S., Little, J. P., Landells, G., Islam, H., Chazaud, B., ... & Krüger, K. (2022). Immunometabolism-fit: How exercise and training can modify T cell and macrophage metabolism in health and disease. *Exercise immunology review*, 28.
- [30] Iyer, A., Brown, L., Whitehead, J. P., Prins, J. B., & Fairlie, D. P. (2015). Nutrient and immune sensing are obligate pathways in metabolism, immunity, and disease. *The FASEB Journal*, 29(9), 3612-3625.
- [31] Newsholme, P. (2021). Cellular and metabolic mechanisms of nutrient actions in immune function. *Nutrition & Diabetes*, 11(1), 22.
- [32] Richter, E. A., & Ruderman, N. B. (2009). AMPK and the biochemistry of exercise: implications for human health and disease. *Biochemical Journal*, 418(2), 261-275.
- [33] Steinberg, G. R., & Hardie, D. G. (2023). New insights into activation and function of the

AMPK. *Nature reviews Molecular cell biology*, 24(4), 255-272.

- [34] Blagih, J., Coulombe, F., Vincent, E. E., Dupuy, F., Galicia-Vázquez, G., Yurchenko, E., ... & Jones, R. G. (2015). The energy sensor AMPK regulates T cell metabolic adaptation and effector responses in vivo. *Immunity*, 42(1), 41-54.
- [35] Liu, X., Niu, Y., Yuan, H., Huang, J., & Fu, L. (2015). AMPK binds to Sestrins and mediates the effect of exercise to increase insulin-sensitivity through autophagy. *Metabolism*, 64(6), 658-665.
- [36] Jiang, S., & Yan, W. (2017). Succinate in the cancer–immune cycle. *Cancer letters*, 390, 45-47.
- [37] Maragkoudakis, P. A., Chingwaru, W., Gradisnik, L., Tsakalidou, E., & Cencic, A. (2010). Lactic acid bacteria efficiently protect human and animal intestinal epithelial and immune cells from enteric virus infection. *International journal of food microbiology*, 141, S91-S97.
- [38] Zhu, M., Kong, F., & Zhao, Q. (2023). Exercise regulates lactic acid metabolism. *Chinese Journal of Tissue Engineering Research*, 27(2), 322.
- [39] Zhang, H., Chen, T., Ren, J., Xia, Y., Onuma, A., Wang, Y., ... & Huang, H. (2021). Pre-operative exercise therapy triggers anti-inflammatory trained immunity of Kupffer cells through metabolic reprogramming. *Nature metabolism*, 3(6), 843-858.
- [40] Sahar Rahimi, Zahra Sayevand, Leli Rezaie Kahkhaie, Tayebah Ahmadi & Atena Alifarsangi. (2025). Exercise and Immune System: A Comprehensive Review in the Era of Coronavirus. *Iranian journal of allergy, asthma, and immunology*, 24(4), 428-440.
- [41] Rongxuan Li, Di Cui, Qingqing Fan, Le Zhao, Ziyao Xia, Tianer Zuo... & Zuoliang Wang. (2025). The impact of 24-h movement behaviors on college students' physical fitness and its isotemporal substitution benefits: a compositional data analysis approach. *BMC public health*, 25(1), 2507.
- [42] Ye Cheng & Yan Song. (2025). Research on the Correlation between Physical Health Diagnosis of College Students and Intervention Mechanism of Exercise Prescription. *Frontiers in Sport Research*, 7(1).