Dear Editor,

Please find enclosed a modified version of my Microreview manuscript “Physical Activity and its Role in Cancer Prevention”. To address the concerns and comments raised by the 4 reviewers, I made the following changes to improve and clarify the manuscript. It is my hope that these changes make the manuscript acceptable for publication in Microreviews in Cell and Molecular Biology.

Sincerely,

Lindsey Scorsone

**Reviewer 1:**

1. I did not agree with all suggestions made by Reviewer 1, but the point about including the organization or people behind/in each study was helpful.
2. From the comments by Reviewer 1, I included the background of people in the cohort/which organizations were carrying out the studies. I also fixed some grammatical errors that were brought up by Reviewer 1. I disagreed with having to put results in table format, as I did not receive any comments from other reviewers that this would be suggested.

**Reviewer 2:**

1. I agreed with all the comments made by Reviewer 2 regarding the quality of my manuscript.
2. After reading the comments from Reviewer 2, I did not change anything in my manuscript because no editing suggestions were made.

**Reviewer 3:**

1. I did not agree with the one and only suggestion made by Reviewer 3. They suggested I add even more information on how to prevent cancer with physical activity.
2. Based on the suggestions made by Reviewer 3, I did not make any edits to my manuscript. I feel that adding more information is going to clog the manuscript and take away from the major facts and points that were made regarding activity and cancer prevention. I wanted the manuscript to be concise and send the message directly.

**Reviewer 4:**

1. I agreed with some of the comments made by Reviewer 4 about adding more information about how activity levels are decreasing in our generation.
2. From the comments Reviewer 4 made about adding information about insufficient activity in our generation, I added some more information in about this to improve my manuscript.

**[Physical Activity and its Role in Cancer Prevention]**

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**Key Words: cancer, prevention, exercise, activity, health, treatment**

Physical activity is being recognized as a prevention mechanism for multiple cancers. There is a great number of studies that have been carried out identifying that the greater amount of physical activity a person partakes in, the less the chance of being diagnosed with cancer is. A few studies have been broken down with their findings and progress associating varying levels of exercise with risk of multiple cancers. It is so important to identify methods that can be done to decrease the risk of cancer, as it is one of the highest causes of death. Not only is physical activity a tool for cancer prevention, but it also influences other aspects of the human body that can contribute to the risk of cancer. These studies have found that most cancers and their risk can be lowered as the amount of physical activity that one participates in increases. With this, there are some that with increasing, high activity, the risk does not change in comparison to moderate activity. Right now, these studies are all coming out with the same findings, exercise truly does make an impact on the prevention of cancer. As research is still coming out, and with the cohort of people that these studies used, a couple problems can arise. How does exercising as a young adult and not just as an older adult affect cancer risk? Also, what are the biological mechanisms that physical activity has on the prevention of cancer? All are open to answer as this topic in cancer is further studied and researched.

**Introduction**

Cancer is one of the largest causes of death all over the world. Specifically, it is the 2nd greatest cause of death in the United States (CDC, 2020). It has been one of the greatest medical battles that professionals have been going against for as long as history goes back, one whose cure has not been completely found universally. There has been continuous research about new methods in cancer, prevention, with one of those simply being physical activity and regular exercise. Cancer is responsible for 1 in 8 deaths all over the world. (Murray, et al., 2020) We know of so many pathogens, foods, and chemicals to stay away from that knowingly cause cancer, but what about proactively doing something to prevent it? How can humans take steps in doing something that is not only healthy for their body but also is able to prevent something that can be extremely detrimental and deadly. Lastly, can physical exercise really make an impact on delaying or even completely preventing cancer? It will be further discussed how the type and amount of activity has shown to influence and lower the risk of multiple types of cancers.

**Recent Progress**

There have been several studies carried out that have proven physical activity to be a method of prevention for multiple types of cancers. One study looked at characteristics of physical activity and its effect on colon and rectal cancers. The participants in this study were between the ages of 50 and 74 years. At the beginning of the study, questionnaires were given to each participant asking about exercise habits and diet habits. About 6 years later, the cohort was recontacted and given another questionnaire to ask about medical history within the last 6 years, any new cancer diagnoses, and exercise amounts. With each increase in total hours of exercise in the cohort of about 150,00 people, the risk of colon cancer decreased in men. Rectal cancer risk decreased in those with moderate total activity, but not those individuals who had immense amounts of activity. Men who had any physical activity versus those who had none had an 18% lower risk of being diagnosed with colon cancer (Chao, et al., 2004). Women who exercised compared to those who did not showed no difference in colon cancer risk, there was no dose-response observed. Walking itself was not enough to just prevent colon cancer, but walking with other recreational activities did. As it was mentioned, moderate amounts of activity proved to be a better method of prevention for rectal cancer than intense amount of activity.

 Physical activity can also have an impact on risk of diagnosis of non-Hodgkin lymphoid neoplasms (NHL), a cancer that begins in your lymphatic system. A study compared amounts of sitting time of a cohort of about 2,000 people and its relation to risk of NHL. This cohort was the American Cancer Society Cancer Prevention Study II Nutrition Cohort. These individuals were given questionnaires asking about medial, behavioral, and diet habits. Every 2 years until the end of the study, the participants would fill out the same questionnaire. In women, those who said they performed even small levels of regular exercise had a 20-30% reduction in risk of these neoplasms compared to women who said they did not do any physical activity (Teras, et al., 2012). Women who had substantial amounts of activity a week had a 48% lower risk of neoplasm diagnosis compared to women with no activity (p=0.008). To further push the significance of these findings comparing activity and cancer risk, women who sat for over 6 hours a day compared to women who sat for less than 3 hours per day had twice the risk to develop NHL. Among men, there was no significant relation between activity and risk of NHL.

 Among another cohort of about 360,000 participants recruited by the UK biobank, cancer types were associated with physical activity levels, low, moderate, and high. Low activity was classified as not meeting the criteria for moderate or high. Moderate activity was classified as at least 20 minutes of vigorous activity 3+ days of the week or 30 minutes or more of moderate activity 5x a week. High levels were classified as at least 3 days a week of vigorous activity for longer amounts of time, or at least 7 days of vigorous activity and walking combined. High levels of activity compared to low levels lowered risks of lung, breast, colon, and hepatobiliary tract cancers. Medium levels of activity were associated with lower risk of oropharyngeal and lung cancers compared to low activity levels (Murray et al., 2020).

 Through each of these studies, there was also supplemental information that those who were at smaller risk for cancer of course exercised more, but had a lower BMI, better eating habits, a greater amount of education, were non-smokers, drank less alcohol, and ate less red meat (Murray et. al, 2020). All of these factors themselves are able to play a part in the onset and progression of cancer.

**Discussion**

More and more Americans everyday are finding hobbies that exclude physical activity: video games, watching tv, monitor gaming systems, and other like activities (Teras, et al., 2012). It was even found that teens who got an hour of exercise each day had a 10% less risk of depression later in their teen years, just another benefit of physical activity (AHA, 2020). Right now, only about 1 in 4 US high school students are getting the recommended 1 hour of activity a day (AHA, 2020). We know that physical activity keeps us sharp, in shape, and fit for survival. Not only do we need to keep up exercising for those reasons, but because it is such an easy way to prevent or help prolong the development of cancer, as it has been discussed in multiple studies. Physical exercise also influences other aspects of our body that can contribute to cancer. Such things are weight, heart health, and the influence of a better diet. The results from these studies provide substantial, valid evidence that even a slight amount of physical activity over none can have an impact on your risk of being diagnosed with cancer. In some cases, with some types of cancers, the more physical activity you do, the less likely you are at risk of the onset of cancer. There are some questions that can arise from these studies. For example, rectal cancer risk decreases with moderate activity, but not with intense activity. There can be questions raised about why more activity than less does not affect and lower cancer risk. These studies also included older adults whose activity level when they were kids and young adults was unknown. We can ask, how does exercising as a young adult early on in live further decrease the risk of cancer (Chao, et al., 2004). This is where longer, more detailed and prolonged studies could come into play. Lastly, what are the biological mechanisms that exercise plays in preventing cancer on the cellular level? All are questions that have still yet to be fully researched and explained.

**References**

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