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Article

# Does Losing Weight Lower the Risk of Cancer: A Systematic Review and Meta-analysis

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**Abstract:** (1) Background: Loss of weight is one of the practices which have been identified as key in reducing the risk of various forms of cancer. Therefore, this study is a systematic review and meta-analysis of studies related to the topic of loss of weight and risk of cancer and addresses the question, 'does losing weight reduce the risk of cancer?' Its purpose is to identify current high-quality evidence on such a question and synthesize such evidence before summarizing it given specific data attributes to improve decision-making processes on cancer management. (2) Methods: Research studies were identified from four main databases: PubMed, Science Direct, Google scholar, and Medline. A systematic review and meta-analysis of such studies were then conducted to reveal the most current evidence on the research topic. (3) Results: The studies showed that losing weight reduces cancer risk. Nonetheless, such intervention is not necessarily effective, especially in cases where patients may be at risk of developing cancer due to other risk factors. (4) Conclusions: The current study concludes that there is a need to implement effective interventions such as physical exercise, dietary restrictions, or both that can be effective in reducing weight to reduce the risk of cancer.

**Keywords:** cancer, losing weight, interventions, physical activity, dietary restrictions, hormones.

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## 1. Introduction

The global healthcare system largely depends on medical research studies due to their role in providing evidence-based practices and interventions that can be effective in reducing mortality and morbidity rates and hospital admissions caused by various health conditions. As one of the most common diseases whose morbidity and mortality negatively affect the global healthcare system, cancer has become one of the most commonly researched topics in various medical research studies. Many such studies are largely concerned about the effective strategies that can be used in managing such health conditions given that there are 1.9 new million cases and 609,360 deaths of cancer that are experienced in the United States. The findings of previous research studies that have been

conducted on the predisposing and precipitating factors of cancer reveal that obesity and overweight play a significant role in increasing the risk of such a condition and exacerbating the severity of its signs and symptoms among patients who have already been diagnosed with it. Such research studies have based their findings on the fact that the trends in the rates of obesity and overweight largely conform to those of cancer. In essence, the researchers of such studies are convinced that around 19.3 million people globally currently have various types, mainly because many of such patients are either overweight or obese, given that 13% of the global adult population is obese and 39% of such population is overweight. On that note, there is a need to determine whether a reduction in the rates of obesity and overweight can be effective in managing the risk of cancer and its related signs and symptoms.

Even though many research studies have identified a positive relationship between cancer and obesity and overweight, there are also those whose main focus has been on losing weight and its influence on the risk of developing cancer. Many researchers of such studies have the notion that the risk of cancer can be significantly decreased if obese and overweight populations implement interventions aimed at losing weight. Some examples of such interventions include physical exercise, weight loss surgeries, and proper diet and nutrition. The content that losing weight results in a decrease in the secretion of a wide range of hormones within the human body, whose main role is to facilitate cell replication, multiplication, and growth which positively affects cancer development. Since cancer, obesity, and overweight are slowly becoming a burden to healthcare systems, it is now the appropriate time to conduct a systematic review and meta-analysis of such research studies to make informed healthcare decisions that can foster the management of such conditions concurrently. On that note, the current study will aim at assessing and synthesizing the findings of research studies that are related to the topic, *'does losing weight lower the risk of cancer?'* and provide an overall summary estimate of their collected data and findings to improve the healthcare decision making processes on the management of various forms of cancer. The study on such a topic hypothesizes that losing weight lowers the risk of cancer. Since cell replication, multiplication and growth are the major reason behind the growth of cancerous cells, limiting such cell processes and activities through interventions aimed at promoting weight loss can positively contribute towards a decrease in the risk of cancer.

## 2. Materials and Methods

### 2.1. Search Strategy and Selection Criteria

In this research study, two main goals were to be achieved by the researchers. Firstly, the researchers aimed to critically appraise and synthesize relevant findings from previous medical research studies to determine whether losing weight leads to a low risk of developing cancer. The preferred medical research studies used explicit and reproducible research methodologies and have both academic and research importance on the such topic in the future. Secondly, the researchers of this study were focused on conducting a statistical analysis of data from such research studies whose focus was to determine whether losing weight lowers the risk of cancer. In this regard, the current study is both a

systematic review and meta-analysis of research studies related to the topic of interest that has been aforementioned because it entailed an assessment of heterogeneous trials from research articles with no summary estimate and an overall summary estimate from available data related to such topic.

A wide range of inclusion criteria was taken into account by the researchers of the current study before their systematic review and meta-analysis. One of them is that all the studies that were included must have been published during the last five years, specifically from November 1, 2017, to November 1, 2022. In this way, it was easier to obtain the most current information and data related to the research topic, thus providing accurate and valid findings. All of such research studies that were included were also to be published in the English language. Furthermore, they had to be focused on populations regarded as either obese or overweight and at risk of developing various forms of cancer due to their weight. Lastly, all the included research studies used randomized controlled trials, which are mainly characterized by the fact that their samples of participants were randomly selected. For that reason, it was possible to decrease the risk of sampling bias which may have negatively affected the credibility and validity of their research findings.

To narrow the search for more relevant research studies related to the topic of interest, it was necessary to exclude some studies for various reasons. One of the exclusion criteria for the studies used in this systematic review and meta-analysis was that non-peer-reviewed articles were not used. That is because such articles were perceived to have been written by less experienced authors, thus affecting the relevancy and validity of their findings. The other exclusion criteria of research studies set for this systematic review and meta-analysis was that all the articles had to be relevant to the research topic by encompassing the subjects of losing weight and the risk of developing cancer. In this way, any research study considered irrelevant to the current study's topic of interest had to be excluded because they were not important in contributing positively to the accuracy and reliability of its findings.

The search process for the research studies used in the current systematic review and meta-analysis involved assessing various databases that were considered useful in finding medical and health research studies and journals. The databases searched were Google Scholar, PubMed, Medline, and Science Direct, and the date cutoffs for the search process for all the studies were between November 1, 2017, and November 1, 2022, as illustrated by chart 1 in the Appendix section below. The search terms that were used for searching research articles from Google Scholar as one of the research databases were '*low weight and cancer*', '*overweight and cancer*', '*obesity and cancer*', '*normal weight and cancer*', '*overweight and cancer risk*', '*obesity and cancer risk*', '*reduced weight and cancer risk*' and '*decreasing obesity and cancer risk*'. Through the use of such terms and the aforementioned inclusion and exclusion criteria, it was possible to identify a significant number of relevant research articles, which were, in turn, used for this systematic review and meta-analysis.

Due to the researchers' need to develop a proper understanding of the scope of the topic of interest, it was necessary to conduct thorough research that entailed assessing various grey literature on such topics. Nonetheless, none of the assessed grey literature was included in the systematic review and meta-analysis and instead provided a

background understanding of what the researchers needed to expect from the included research studies. Some of the grey literature that was used included theses, blogs, white papers, and podcasts that were related to the topic of weight reduction and the risk of cancer. Despite the thorough search process for the relevant research studies, trial registries were not searched, and data was not obtained from unpublished studies on the topic of interest. Furthermore, the data that was largely sought after by the researchers of this study were individual patient-level data due to their accuracy and preciseness in answering the distinct research questions and hypotheses of the chosen studies. On that account, none of the findings of the research studies included in this systematic review and meta-analysis entailed summary estimates of their data collected on the current topic of interest.

Due to the complexity associated with a systematic review and meta-analysis, collaborative efforts are often necessary to achieve such research activities' intended goals and objectives. On that note, the authors of the current study, whose names have been mentioned above, were fully responsible for undertaking the research articles' search and data extraction processes and activities. However, in case of conflicts that arose on the inclusion of research articles, a third party acting as a reviewer of this study who is highly skilled and knowledgeable in medical and nursing sciences was obligated to determine whether research articles whose inclusion was associated with a conflict of interest were to be included or excluded. The inclusion criteria for the systematic review and meta-analysis were the same and involved randomized controlled trials focused on the topic of losing weight and the risk of cancer that had been published in English within the last five years. Lastly, the current study's protocol is not yet available online, and no link can be provided for it.

## 2.2. Data Analysis

The ability of the researchers of any systematic review and meta-analysis to achieve the goals and objectives of their research studies mainly depends on the efficacy of their data extraction methods and the ability to recognize and properly deal with duplicated data. For this study, a logical method of data extraction was undertaken, which implies that all the data was extracted from the source system at once in order to save on research labor and time. The specific logical method of data extraction that was undertaken was a full extraction in which data all data was extracted from one source before the extraction process commenced in another source of literature. To deal with duplicate data, similarities in the research hypotheses and questions of the studies that were to be included had to be identified. In the event that the similarities also resulted in similar research findings with statistical significance and corresponding influence on research questions and hypotheses, only one of the research studies had to be chosen for the systematic review and meta-analysis. In this manner, it was possible to decrease the risk of data duplication, which may have negatively affected the efficacy of the current study in meeting its medical importance and significance.

The primary outcome of the research studies that were analyzed could be categorized into two main types. Some of the research studies focused on the outcome of the number of participants whose weight increased their risk of developing various forms of cancer. Another set of the included studies focused on a primary outcome of the number

of participants whose weight decreased their risk of developing various forms of cancer. The measured effect for the research studies that were analyzed was a risk ratio involving a comparison of the risk of developing cancer by participants of diverse weights and Body Mass Indices (BMIs). The overall risk ratio for the research studies was 1.2 at a 95% Confidence Interval (CI) which implies that people who had lost weight were just 20% more likely to develop cancer which is significantly low. The odds of developing cancer were also measured using an odds ratio at a 95% confidence interval. The average odds ratio (OR) of the included research studies was 1.9, implying that the odds of developing cancer among participants who could not lose weight were 90% higher than among those who could. There were also two preplanned secondary outcome measures of the included research studies. One of them was the severity of the various forms of cancer that participants were susceptible to, depending on their weights. The other was the extent to which the decrease in the weight of the participants due to the implementation of specific interventions decreased their risk of developing specific types of cancer. Lastly, there were no adverse events experienced during the randomized controlled trials conducted by the researchers of the included studies. Consequently, none of the research studies played a role in placing participants at risk of weight gain or developing cancer.

Other than the implementation of the inclusion and exclusion criteria for the research articles used in this systematic review and meta-analysis, it was necessary to undertake a risk of bias assessment for the included studies. The Johns Hopkins Nursing Evidence-Based Practice (JHNEBP) evidence level and quality guide toolkit was used for determining the quality of the research processes and findings of the included articles. Using such a toolkit and relying on the study designs of the included research studies, it was possible to determine whether their findings were of high, good, or low quality, as shown by Table 2 in the Appendix section below. The research studies with a high or good quality were considered to be at low risk of having biased findings, while those with low evidence quality were considered to have a high risk of biased findings. However, sensitivity analyses were not done after the exclusion of studies at high risk of bias since there were very many such studies. Therefore, sensitivity analyses required more labor and time resources which were not available for the researchers.

Based on the research topic of interest, data were extracted from two variables in all the research studies included for the analysis. The independent variable in some of the research studies was the risk of developing cancer which was the health signs and symptoms which signified a likelihood of developing any form of cancer by the participants sooner or later. The dependent variable for many of the research studies was the participants' weight, which was the actual measure of the quantity of matter that forms the physiological aspects and tissues of the participants. Since the systematic review and meta-analysis were not interested in summary estimates data, no summary measures were used by the included research studies. The variability between and within the studies was assessed using heterogeneity which was measured using an  $I^2$  index to demonstrate the percentage of total variability within the methods and findings of such studies. The average  $I^2$  for the included research studies in this systematic review and meta-analysis was 23%, demonstrating a small heterogeneity and variability in their findings. Studies were

combined based on the nature of their model parameters. In essence, studies with non-random quantities were combined before assessing the differences in their research methodologies and findings. In this way, the current systematic review and meta-analysis used a fixed effects model to synthesize and summarize the studies' statistical findings. Due to the quantitative nature of the synthesized research studies, an accurate data analysis package was necessary. The statistical package that was used by the researchers of the analyzed studies was Statistical Package for Social Sciences (SPSS), and its version number was 1.0.0.1406. Lastly, the current study still lacks a registration number and is yet to be registered in any of the medical registries for systematic reviews and meta-analyses.

### 2.3. *Role of the Funding Source*

Due to the labor and time resources that are necessary for conducting systematic reviews and meta-analyses, the researchers of such studies usually seek funding sources to meet the goals and objectives of their studies in a more precise manner. Nevertheless, no stakeholder with a funding role impacted the study design, data collection, analysis, interpretation, and writing of this research report. As such, there was no funding source for this study, and all its financial needs were left as the obligations of its researchers.

## 3. Results

For the current systematic review and meta-analysis, 100 research articles related to the topic of interest were assessed for eligibility and screened. However, after implementing the inclusion and exclusion criteria, 40 research articles were included in the current study. A total of 58 research articles were considered ineligible since they were not peer-reviewed, not published within the last five years, or included abstracts and not full-texts, as shown by Chart 2 in the Appendix section below. Consider the study selection figure 1, shown in the Appendix below that, which is based on the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. All the research articles that were used in the current study used a randomized controlled trial as their research design. However, 11 of the chosen research articles were population cohort studies, while the remaining 29 were retrospective cohort studies. The sample sizes for research studies used ranged between 500 and 65,800 participants. The interventions used in the research studies include physical exercise, dietary restrictions, or both. Many of the participants in the research studies were adults whose ages were between 18 and 65 years. Consider the summary table 1 in the Appendix section below, which shows the main characteristics of the research studies from which data were extracted.

Due to the current and peer-reviewed nature of the included research studies, they had an accurate and valid primary assessment and secondary findings. There were two main findings for the primary assessment of the included research studies. Firstly, the studies revealed that a decrease in weight results in a corresponding decrease in the risk of cancer [1 (59), 2 (3245), 3 (124), 4 (1325), 5 (14), 6 (1194), 7 (1650), 8 (3), 9 (792), 10 (605), 11 (7), 12 (693), 13 (1799), 14 (87), 15 (499), 16 (70)]. Secondly, the studies revealed that losing weight may not necessarily lead to a lower risk of cancer, especially if other factors such as genetics and lifestyle can still play a role in increasing the such risk [28 (194), 29 (35), 30 (1010), 31 (3), 32 (832), 33 (3762), 34 (3363), 35 (684), 36 (5), 37 (470), 38 (259), 39

(158), 40 (22)]. Similarly, the research studies had two main secondary findings. One of them was that interventions aimed at reducing weight in participants can be effective in addressing the prevalence of cancer among populations [26 (2494), 27 (3583)]. The other secondary finding was that losing weight may curtail the prevalence of precipitating and predisposing factors associated with various forms of cancer [17 (1174), 18 (2493), 19 (523), 20 (5), 21 (1403), 22 (69), 23 (23), 24 (109), 25 (1541)]. Such findings were based on a heterogeneity score of  $I^2 = 23\%$  between and within the findings of the included research articles, which implies that there was little variability in their findings based on their research questions and hypotheses. A total of 37 research studies were considered to have a low risk of bias based on an assessment of their evidence quality using the JHNEBP toolkit. In essence, only 3 of the chosen research articles had low research evidence quality. The risk of bias in the studies was determined using the methodological steps illustrated in Figure 2 below. Finally, as aforementioned, no post-hoc or sensitivity analyses were conducted due to the high number of research articles screened and included in this systematic review and meta-analysis.

Since this study also entailed an overall summary estimate of available data on the research topic stated above, it was necessary to provide a meta-analysis forest plot to provide a simple summary of data for each of the research studies that met the inclusion criteria. Therefore, Figure 1 in the Appendix section below shows a meta-analysis forest plot for the included research studies with a 95% CI for the statistical data of their analyzed research findings. The overall risk ratio of the research studies based on a 95% CI was 1.2. The study with the highest risk ratio was Bowers et al. (2021), whose risk ratio was 1.7, implying a 70% possibility of cancer development among participants who had implemented loss of weight interventions. On the contrary, the study with the lowest risk ratio was Harvie et al. (2019), whose risk ratio was 1.05, implying a 5% risk of developing cancer among participants who had implemented loss of weight interventions during the period of study. Given that 40 research articles were used for this systematic review and meta-analysis, it was of significant importance to determine the total number of research participants for such articles. The total number of participants included in the research studies described in such articles was 1,760,900, which is significantly high and justifies that the findings of this systematic review and meta-analysis are accurate and valid. Finally, the quantitative nature of the research studies demanded the use of probability value (p-value) to determine the statistical significance of their findings based on their research questions and hypotheses. The average p-value for the research articles that met the inclusion criteria was  $p = 0.53$ . Nevertheless, the statistical significance threshold for the research studies was  $p < 0.05$ , implying that the findings of many of the research studies were statistically significant. In this regard, many of the researchers of the articles that were included in this systematic review and meta-analysis did not reject their null hypotheses, which led to their overall finding that losing weight indeed lowered the risk of developing cancer.

**Table 1:** Main Characteristics of the Research Studies Used.

Main Characteristics			
Research Studies	Type of Research Study Conducted	Interventions Used	Participants' Age Groups
Adams et al., 2018	Retrospective Cohort	Physical exercise	18-40
Atakpa et al., 2021	Population cohort	Dietary restrictions	18-54
Avgerinos et al., 2019	Retrospective Cohort	Physical exercise	18-56
Befort et al., 2020	Retrospective Cohort	Physical exercise	20-54
Bowers et al., 2021	Retrospective Cohort	Physical exercise	21-67
Chan et al., 2019	Retrospective Cohort	Dietary restrictions	18-50
Christakoudi et al., 2021	Retrospective Cohort	Dietary restrictions	18-45
Duggan et al., 2022	Retrospective Cohort	Physical exercise	19-45
Friedenreich et al., 2021	Retrospective Cohort	Physical exercise	20-70
Hardefeldt et al., 2018	Retrospective Cohort	Dietary restrictions	15-65
Harvie et al., 2019	Retrospective Cohort	Physical exercise	19-65
Hendifar et al., 2019	Retrospective Cohort	both	18-40
Jensen et al., 2018	Retrospective Cohort	Dietary restrictions	25-55
Kim et al., 2019	Population cohort	Physical exercise	20-65
Klein, 2021	Retrospective Cohort	both	18-70
Lake et al., 2022	Retrospective Cohort	Dietary restrictions	19-54
LeBlanc et al., 2018	Population cohort	Physical exercise	18-45
Ligibel et al., 2019	Retrospective Cohort	Physical exercise	17-55
Ligibel et al., 2022	Retrospective Cohort	Dietary restrictions	20-60
Lope et al., 2019	Population cohort	Physical exercise	Above 21
Lorenzo et al., 2021	Population cohort	Physical exercise	23-65
Luo et al., 2020	Population cohort	Physical exercise	25-65
Moy et al., 2018	Population cohort	Dietary restrictions	25-40
Nicholson et al., 2021a	Retrospective Cohort	Physical exercise	15-60
Nicholson et al., 2021b	Retrospective Cohort	Physical exercise	15-65
Nicholson et al., 2022	Retrospective Cohort	Physical exercise	20-60
Nierengarten et al., 2022	Retrospective Cohort	Physical exercise	25-70
Schembre et al., 2022	Retrospective Cohort	Physical exercise	25-45
Schenk et al., 2019	Population cohort	Dietary restrictions	18-65
Schwalb et al., 2022	Retrospective Cohort	Physical exercise	19-60
Stroud et al., 2019	Retrospective Cohort	both	20-65
Tahrani et al., 2022	Retrospective Cohort	both	15-45
Tao et al., 2020	Population cohort	Physical exercise	Above 18
Trape et al., 2021	Retrospective Cohort	Physical exercise	15-55
Ulrich et al., 2018	Population cohort	Physical exercise	18-60
Wang et al., 2022	Retrospective Cohort	Physical exercise	20-65
Wilson et al., 2021	Population cohort	Physical exercise	20-70
Wood et al., 2021	Retrospective Cohort	Physical exercise	18-70
Xu et al., 2018	Retrospective Cohort	Physical exercise	18-75

Yuan et al., 2020	Retrospective Cohort	Physical exercise	15-65
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### Full Search Terms for One Database (Google Scholar)

1. Low weight and Cancer.
2. Overweight and Cancer.
3. Obesity and cancer.
4. Normal weight and cancer.
5. Overweight and cancer risk.
6. Obesity and cancer risk.
7. Reduced weight and cancer.

**Table 2.** *Risk of Bias Assessment According to JHNEBP toolkit*

Research Studies	Research Evidence Quality	Risk of Bias
Adams et al., 2018	High	Low
Atakpa et al., 2021		Low
Avgerinos et al., 2019	High	Low
Befort et al., 2020	High	Low
Bowers et al., 2021	High	Low
Chan et al., 2019	High	Low
Christakoudi et al., 2021	High	Low
Duggan et al., 2022	High	Low
Friedenreich et al., 2021	High	Low
Hardefeldt et al., 2018	Good	Low
Harvie et al., 2019	Good	Low
Hendifar et al., 2019	High	Low
Jensen et al., 2018	Low	
Kim et al., 2019	High	Low
Klein, 2021	High	Low
Lake et al., 2022	Low	
LeBlanc et al., 2018	High	Low
Ligibel et al., 2019	High	Low
Ligibel et al., 2022	High	Low
Lope et al., 2019	Good	Low
Lorenzo et al., 2021	High	Low
Luo et al., 2020	High	Low
Moy et al., 2018	Low	
Nicholson et al., 2021a	High	Low
Nicholson et al., 2021b	High	Low
Nicholson et al., 2022	High	Low

Nierengarten et al., 2022	High	Low
Schembre et al., 2022	High	Low
Schenk et al., 2019	High	Low
Schwalb et al., 2022	High	Low
Stroud et al., 2019	High	Low
Tahrani et al., 2022	High	Low
Tao et al., 2020	High	Low
Trape et al., 2021	High	Low
Ulrich et al., 2018	High	Low
Wang et al., 2022	High	Low
Wilson et al., 2021	Good	Low
Wood et al., 2021	Good	Low
Xu et al., 2018	High	Low
Yuan et al., 2020	Good	Low

#### List of Studies Excluded at Full Text Screening Stage

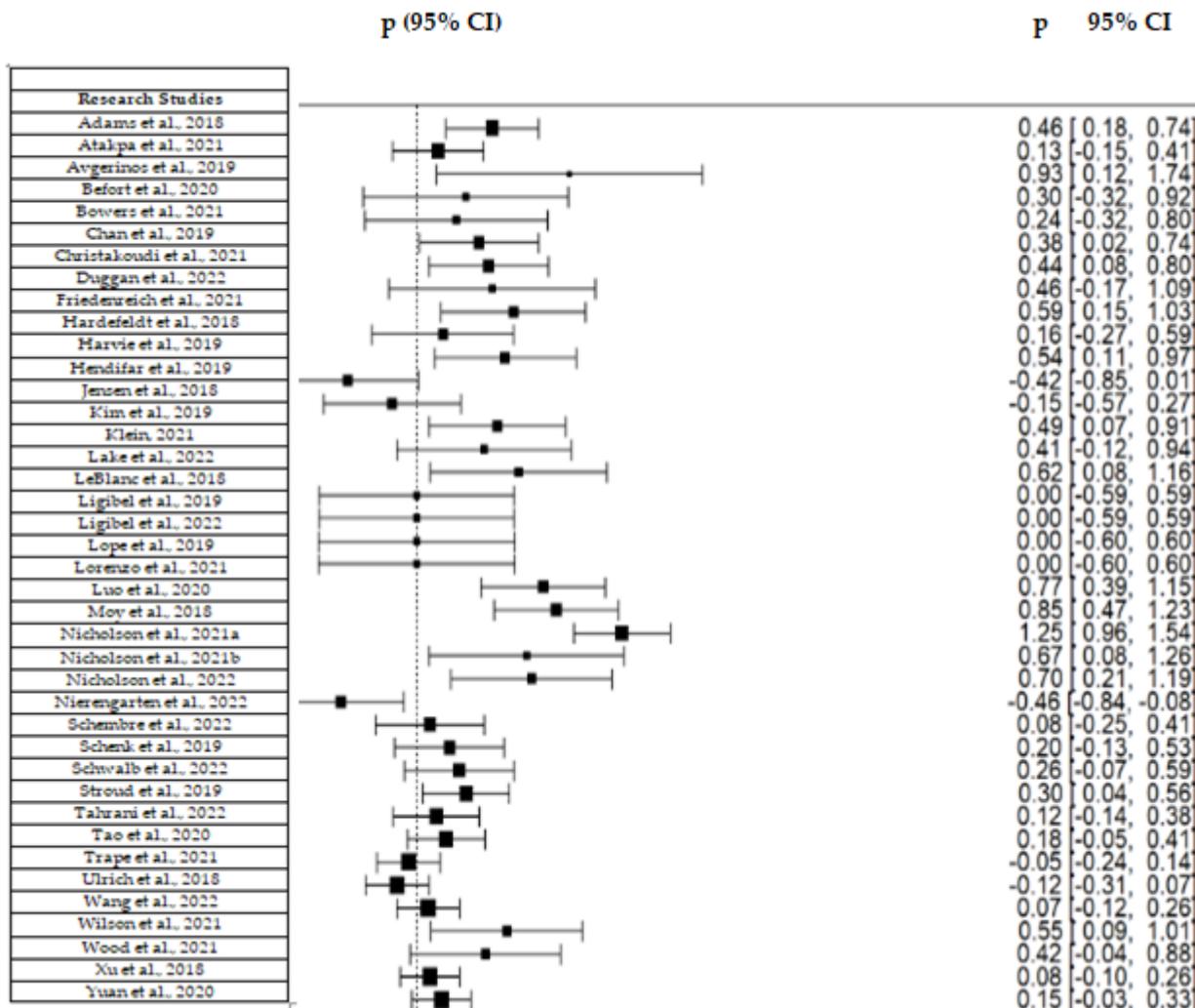
- da Silva, M., Weiderpass, E., Licaj, I., Lissner, L., & Rylander, C. Excess body weight, weight gain and obesity-related cancer risk in women in Norway: the Norwegian Women and Cancer study. *British journal of cancer*, **2018**, 119(5), 646-656.

**Reason for exclusion:** Not a randomized controlled trial study

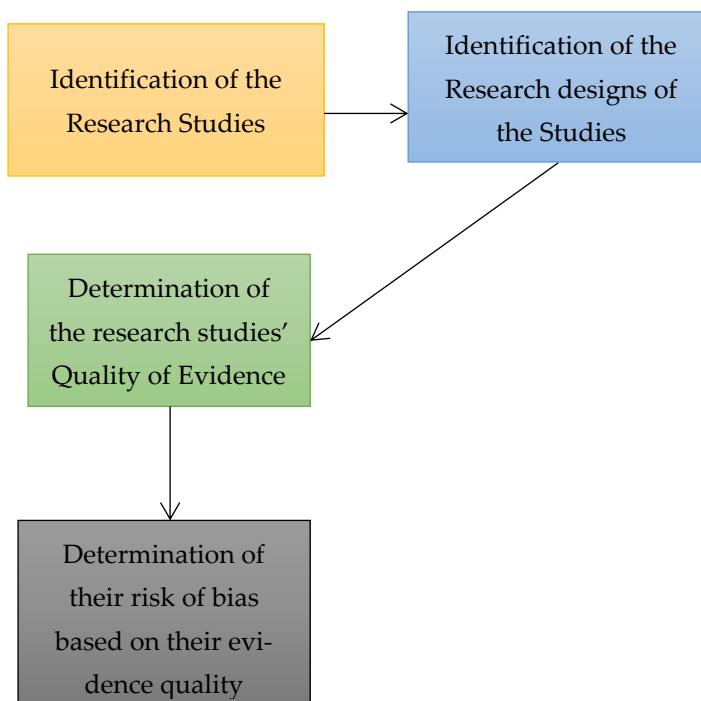
- Weihe P, Spielmann J, Kielstein H, Henning-Klusmann J, Weihrauch-Blüher S. Childhood obesity and cancer risk in adulthood. *Current obesity reports*. **2020**, 9(3), 204-12.

**Reason for exclusion:** Insufficient information on losing weight and cancer risk

**Figure 1.** Meta-Analysis Forest Plot for the Included Studies.



**Figure 2.** Risk of Bias Assessment Methodological Steps Using the JHNEBP Toolkit.



## 4. Discussion and Conclusion

### 4.1. Summary of the Main Findings

From a synthesis and summary of the findings of the research articles that were included in the current systematic review and meta-analysis, there are two main findings that can be made about the topic of research. One of them is that loss of weight results in a corresponding decrease in the risk of cancer [26 (2494), 27 (3583), 28 (194), 29 (35), 30 (1010), 31 (3)]. Such a finding is in agreement with the null hypothesis of the current study and is based on accurate data that have already been published in the included research articles. The main reason why a decrease in weight leads to a corresponding decrease in the risk of developing cancer is that a decrease in weight reduces the level of specific hormones that results in high cancer risk within the human body [26 (2494), 27 (3583), 28 (194), 29 (35), 30 (1010), 31 (3)]. Such hormones include insulin, estrogen, and androgen [28 (194)]. Unlike various hormones that are secreted by the endocrine system, insulin leads to an increase in the production of human cells when secreted in large quantities by the pancreas [1 (59), 2 (3245), 3 (124), 4 (1325), 5 (14), 6 (1194), 7 (1650), 8 (3), 9 (792), 10 (605), 11 (7), 12 (693), 13 (1799), 14 (87), 15 (499), 16 (70), 17 (1174), 18 (2493)]. Furthermore, it reduces cell death despite promoting the physiological processes that enhance cell multiplication and production. In this manner, insulin may exacerbate the development of cancerous cells whenever they begin to develop, which in turn quickens the process of cancer development [32 (832), 33 (3762), 34 (3363), 35 (684), 36 (5), 37 (470), 38 (259), 39 (158), 40 (22)].

Since interventions such as dietary restrictions and physical activity aimed at reducing weight also lead to reduced insulin secretion, there is a decrease in cell multiplication and production in obese or overweight people who are losing weight. In this regard, they become highly likely to reduce their risk of experiencing faster growth of cancerous cells.

Just like insulin, estrogen and androgen are the other hormones secreted by the human endocrine system, which also play a significant role in the development of various forms of cancer. In healthy cells, both estrogen and androgen play the role of aiding normal cell function and growth. The secretion of such hormones in large quantities thus results in healthy cells becoming cancerous due to the inflammation that consistent cell function and growth cause on various organs and tissues within the human body system [19 (523), 20 (5), 21 (1403)]. As a result, estrogen and androgen play a significant role in the multiplication and spread of cancerous cells [20 (5)]. Through weight reduction interventions, there is a decrease in the sensitivity of the endocrine system to secrete such hormones [22 (69), 23 (23), 24 (109), 25 (1541)]. They are thus secreted in low quantities, leading to the monitoring of the consistency of cell functioning and growth by various body systems to avoid the inflammation of body organs and tissues [24 (109)]. On that account, weight loss reduces the secretion of such hormones, resulting in a corresponding decrease in the multiplication and spread of cancerous cells.

Besides weight reduction leading to a low risk of cancer, the other main finding established from the systematic review and meta-analysis of the included articles in this study was that weight loss might not necessarily decrease the risk of cancer in certain people. That occurs mainly if such people are already at a high risk of developing various

types of cancer due to factors such as genetics and lifestyle [17 (1174), 18 (2493)]. For example, a smoker may not necessarily experience a reduction in the risk of developing cancer of the lungs or esophagus even after the implementation of weight reduction strategies such as physical activity and proper diet [32 (832), 33 (3762), 34 (3363), 35 (684)]. Furthermore, the inheritance of a faulty gene, such as the BRCA genes from family members, can increase the risk of developing breast and ovarian types of cancer [22 (69), 23 (23)]. On that account, implementing interventions aimed at weight loss may not necessarily decrease a person's risk of developing such types of cancer.

#### *4.2. Limitations and Strengths of the Research Study*

The current study was associated with two limitations that may have negatively impacted its ability to answer its research question and hypothesis. One of such limitations is that it only included randomized controlled trials to collect quantitative data. As such, there is a possibility that changing attitudes of key stakeholders, such as patients and healthcare practitioners, on the topic of interest may not have been captured during the systematic review and meta-analysis. The other limitation is limited access to data, given that the researchers only used studies from four databases. The limited access to data was attributed to the fact that many medical databases require paid subscriptions for access to certain research studies and articles. Therefore, due to the lack of a funding source, it was not possible to access such databases, leading to a systematic review and meta-analysis of a limited number of research studies on the topic of research.

Two strengths are associated with the current systematic review and meta-analysis. One of such strengths is that the search for the studies was limited to those that were published during the last five years. In this regard, there is a high likelihood that the current study captured any significant changes that may have positively or negatively impacted the findings of research studies conducted more than five years ago. The other strength of the current study is that all the articles used were published in English. As such, the findings are internationally binding in that they can be used for academic and research purposes by all researchers and students regardless of their ethnic backgrounds or nationality.

#### *4.3. Controversies Raised by this Research Study*

Two main controversies are raised by the current study. Given that losing weight decreases the risk of developing various forms of cancer, it is questionable whether low weight is associated with a low risk of cancer. On that note, one of the controversies raised by the current systematic review and meta-analysis is whether people with low weights and BMIs are at low risk of developing cancer. Another controversy raised by the current research study is whether losing weight can be an effective strategy for managing cancer-related signs and symptoms. From the analysis of the findings of the research articles that were included in this systematic review and meta-analysis, it was revealed that losing weight decreases the spread and multiplication of cancerous cells. Therefore, it is questionable whether the such strategy can be effective in reducing the risk of the severity of the signs and symptoms associated with various forms of cancer. However, despite such controversies, there are no discrepancies in the findings of this study with other systematic reviews and meta-analyses related to the research topic. In this way, there is a high

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level of certainty regarding the accuracy of the systematic review and meta-analysis and the findings of the included research studies.

#### 4.4. *Suggestions for Future Research Directions*

Based on the controversies that this systematic review and meta-analysis have raised, there is a need for future research studies to focus on two main topics. One such topic is the effect of low weight on the risk of developing cancer. The other is the effectiveness of losing weight in managing the risk of cancer and its related symptoms. Through synthesis and summary of the findings of studies that are related to such topics, future systematic reviews and meta-analyses can enhance the understanding of the relationship between losing weight and the risk of developing cancer in a more significant manner to patients and healthcare practitioners.

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#### Appendix

**Chart 1: Databases Used for Identifying the Research Articles.**

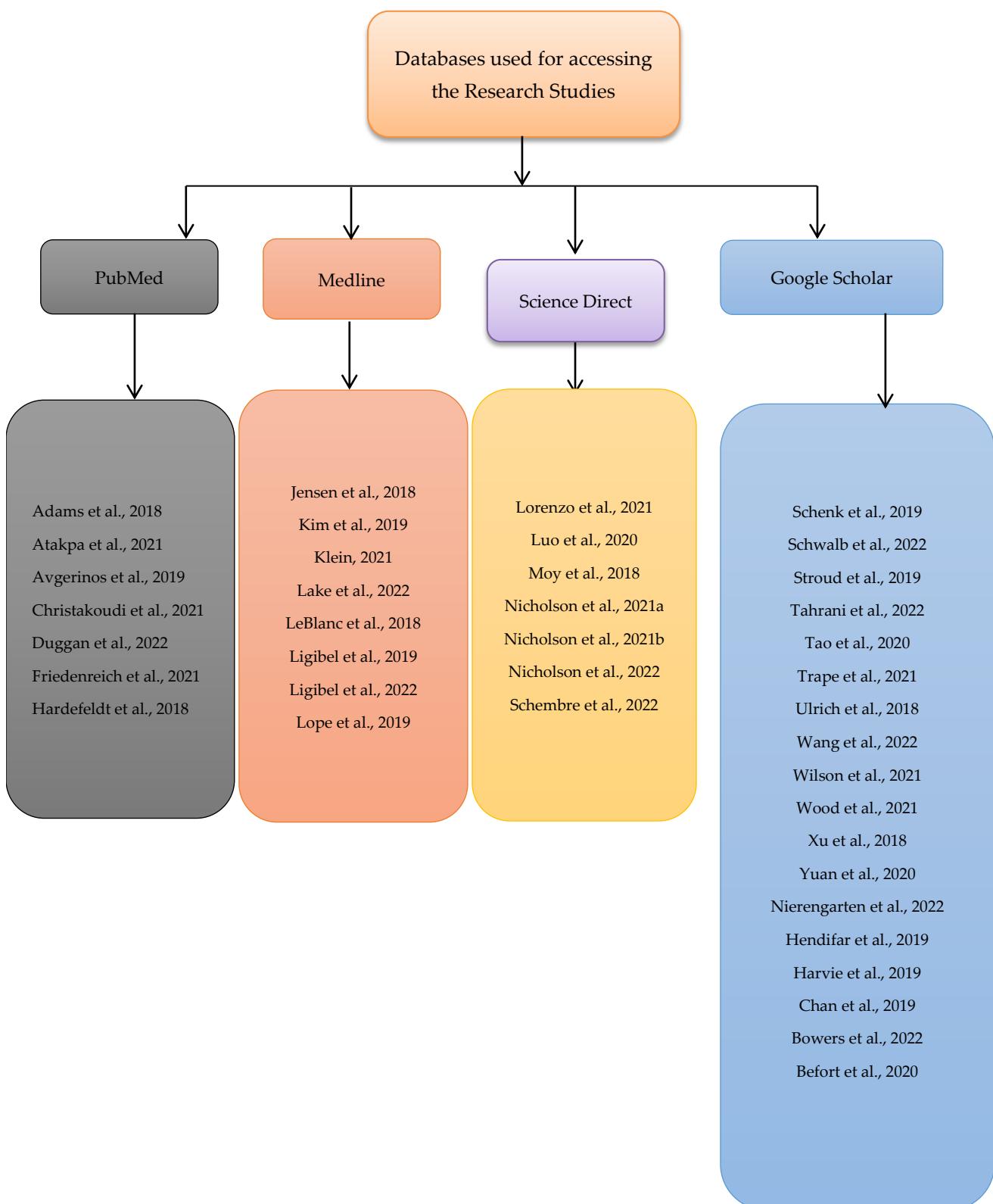
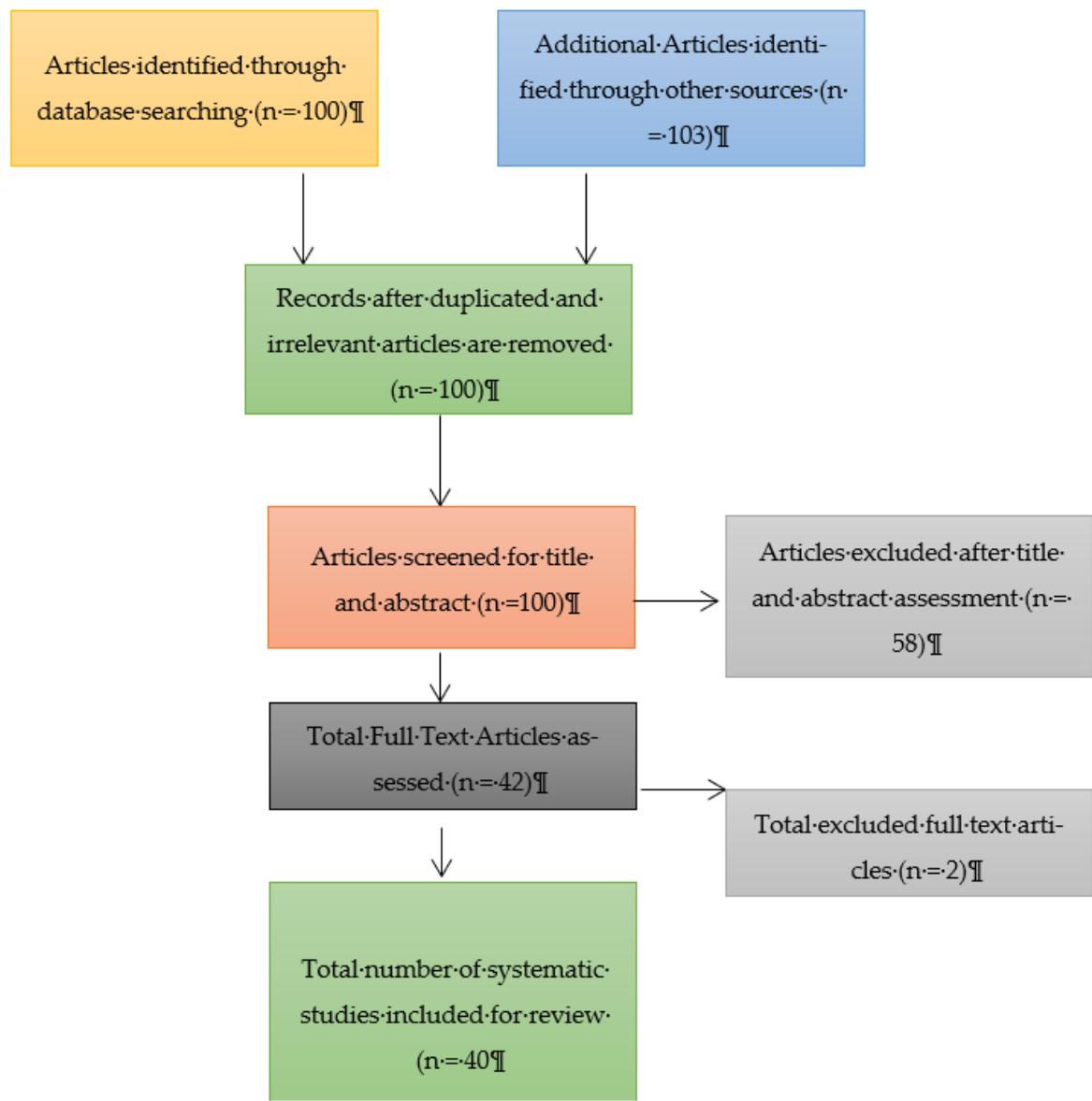


Chart 2: Study Selection Figure for the Systematic Review and Meta-Analysis.



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