The impact of BMI on Ovarian Cancer- An Updated Systematic Review and Metanalysis

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Simple Summary: Ovarian cancer is becoming increasingly common, with medical experts claiming that its prevalence rates could be attributed to many people's high Body Mass Indices (BMIs). Therefore, it was necessary to determine the influence of BMI on ovarian cancer by conducting a systematic review and meta-analysis of previous research studies related to the topic. The current study involves a synthesis of the findings of 20 research studies published in English within the last five years and related to the topic. Research studies were obtained from four databases: the Cochrane Library, PubMed, Google Scholar, and Science Direct. According to a systematic review and a meta-analysis of the findings of such articles, it is established that an increase in BMI not only boosts the risk of developing ovarian cancer but also the severity of the condition.

Abstract: A significant number of research studies have focused on determining whether BMI influences various types of cancer. The findings of these studies showed that people have to manage their BMIs to decrease their risk of developing various types of cancer, one of which is ovarian cancer. A PRISMA guideline for systematic review and meta-analysis was used to identify 20 research studies related to the topic to establish the truth or falsity of the findings. Later, their findings were synthesized. The synthesis of the findings of such research articles suggests that overweight and obese increase an individual's risk of developing ovarian cancer and experiencing severe symptoms of the disease. In such a manner, the current research study can conclude that effective management of BMI is necessary for decreasing the prevalence and mortality rates associated with ovarian cancer.

Keywords: ovarian cancer; BMI; obesity; overweight; normal weight; statistical significance

1. Introduction

Many healthcare systems around the world have focused on developing effective clinical strategies and interventions aimed at reducing the prevalence and mortality rates caused by cancer. Since cancer is the second leading cause of death in the United States, it is crucial to implement measures that can reduce the rates of various types of cancer, especially those related to human reproductive health [1] (p.184). It is estimated that 40% of all cancers diagnosed in the United States every year are caused by obesity, which is characterized by a high Body Mass Index (BMI) of more than 30kg/m^2 [2] (p.23). Charts 1 and 2 show the prevalence rates of obesity and ovarian cancer in the United States, respectively. For that reason, the topic of the current research study is important because proper management of BMIs of diverse populations in the United States can reduce the prevalence and mortality rates caused by cancer by up to 40% [2] (p.23). Due to the relationship between BMI and cancer diagnoses, the current study aims to assess the influence of BMI on ovarian cancer as one of the thirteen types of disease associated with overweight and obesity, following Figure 1 below. Consequently, this study is significant since it strives to justify the need for proper management of BMIs of representatives of diverse

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populations to decrease their risk of developing ovarian cancer and experiencing severe symptoms of this health condition.

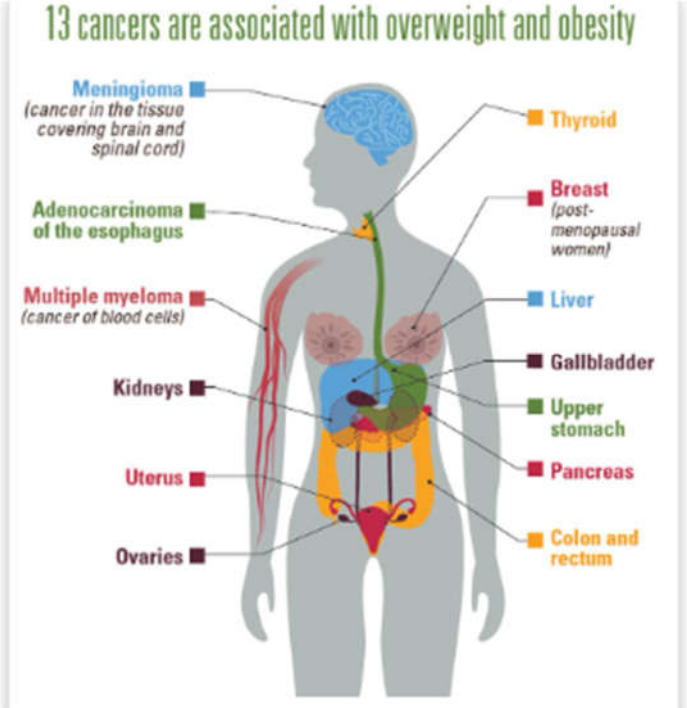

Figure 1. 13 Types of Cancer Associated with Overweight and Obesity. Source: (Center for Disease Control, 2022).

A significant number of research studies have analyzed the relationship between a high BMI, specifically obesity and overweight, and various types of cancer. A high BMI is considered to be associated with an increased amount of adipose tissue that results in an excessive amount of estrogen as a reproductive hormone in females [3] (p.490). In the case of normal physiological functions, the process of eliminating excess estrogen from the human body involves metabolically converting such hormones to inactive metabolites after their hydroxylation, which is catalyzed by cytochrome P450 enzymes [4] (p.123). However, a high BMI often hinders the process of elimination of excess estrogen from the body due to its effects on the physiological processes related to the removal of hormones and enzymes as human waste [5] (p.1). In this manner, a high BMI leads to increased secretion of estrogen and hinders the process of eliminating it from the body. In turn, it leads to the deposition of estrogen around ovaries, thus resulting in ovarian cancer with negative symptoms presented in Figure 2 below [7] (p.1102). The primary aim of the current study is to undertake a systematic review and meta-analysis of various articles related to the research topic in order to determine the most accurate and valid evidence. Through an analysis of such evidence, it is possible to conclude that managing obesity is necessary for decreasing cancer prevalence and mortality rates. Due to the positive relationship between an increase in BMIs in the population and a rise in the rates of ovarian cancer, the implementation of available clinical evidence sourced from a systematic review and meta-analysis of research studies on the influence of BMI on ovarian cancer can enhance proper management of morbidity and mortality related to this type of cancer.

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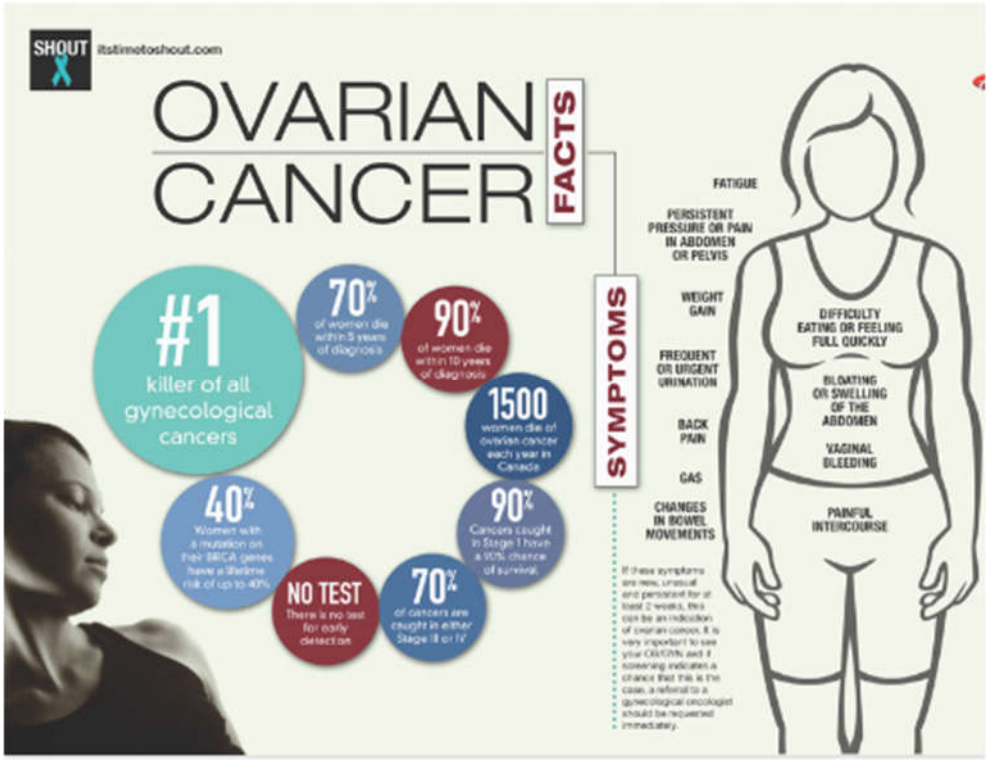

Figure 2. Symptoms of Ovarian Cancer. Source: (Chu et al., 2018, p.1098).

2. Materials and Methods

2.1. Study Design

As a systematic review and meta-analysis, this research study was guided by a secondary quantitative research design and specifically used Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) shown in Chart 3 below for conducting the systematic reviews and meta-analysis of already published research articles on the topic. The relevancy of the articles depended on whether they involved randomized trials and were significantly related to the topic of interest. The eligibility of full-text research articles was then undertaken before the identification of their inclusion and exclusion for the purpose of the systematic review and meta-analysis. Resultantly, the use of PRISMA guidelines for conducting the systematic review and meta-analysis enhanced the transparency and credibility of the findings discussed in the current research study.

2.2. Search Strategy

The accuracy of the findings discussed in the current research study was mainly attributed to various literatures that were used for the systematic review and meta-analysis. Consequently, it was necessary to identify such articles from various databases, including PubMed, Cochrane Library, Science Direct, and Google Scholar, as shown in chart four below. The search process involved using keywords and phrases that were relevant to the research topic to search for the research articles from such databases. The keywords and phrases that were used include 'obesity,' 'overweight,' 'high Body Mass Index, 'adiposity,' 'ovarian cancer,' 'weight gain and ovarian cancer,' 'ovarian cancer risk factors, 'carcinoma,' and 'epithelial tissues. Only articles that were published during the last five years until 31st October 2022 were used. Lastly, a screening of the bibliographic sources of the articles was undertaken to ensure that they were approved for academic and research purposes. In this way, it was possible to achieve the relevancy of the findings of this research study in meeting the goals and objectives of future similar studies related to its topic of interest.

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2.3. Inclusion and Exclusion Criteria

Even though the relevant keywords and phrases mentioned above were useful in obtaining a significant number of research articles, it was necessary to implement specific inclusion and exclusion criteria to determine the most relevant ones for the systematic review and meta-analysis. The most important inclusion criterion was that the research articles must have been published within the last five years to obtain the most accurate and current evidence on the research topic. Additionally, all the research articles that were used for the systematic review and meta-analysis were published in English only. In this way, there was sufficient confidence that such articles were approvable and useful on an international scale.

Even though the databases had a significant number of articles that were relevant to the research topic based on the use of the key relevant words and phrases to search for them, they had to be excluded for various reasons. Articles that lacked full text and only included an abstract were excluded because their findings could not be justified as sufficient to meet the objectives of the current study. Furthermore, articles with little to no information on BMI and ovarian cancer were excluded since they were regarded as less relevant to the topic of interest in the current study. On that account, the implementation of such inclusion and exclusion criteria was significant in improving the efficiency of the current study to rely only on the most current evidence-based findings related to the research topic to achieve its purpose.

2.4. Article Screening

A screening of the articles that were used for the systematic review and meta-analysis was pertinent to the current research study since it justified the applicability of such articles for meeting different academic and research needs. The article screening process was undertaken shortly after the implementation of the inclusion and exclusion criteria mentioned above. Two authors of this study participated in the article screening process, and an unbiased third party with sufficient skills and experience in the field of nursing and medicine addressed any contradictions that the authors had during the screening process. The process of screening the articles involved three main activities that were all undertaken by the authors. First, the authors assessed the titles of the research articles that had met the inclusion criteria to determine whether they were relevant and not complex for academic and research purposes. Second, the authors read the abstracts of the research articles to determine whether their research methodology, findings, and discussion aligned with the evidence that was intended for this research study. Finally, the authors assessed whether the research articles were either edited, peer-reviewed, or both. For that reason, there was a high level of confidence that the researchers and authors of such research articles were experts in the field of medicine, which implied that such research articles were only based on sound facts and not conjectures that were yet to be proven.

2.5. Data Extraction

The extraction of data and pertinent information related to the research topic was undoubtedly the most important research activity necessary for achieving the goals and objectives of the systematic review and meta-analysis conducted. It involved two authors of the current research study acting as reviewers of the included articles. One of the authors was responsible for extracting full data and information from the research articles' methodology, findings, and discussion sections, while the other independently checked whether the extracted data and information were accurate and complete in achieving the purpose of the research study. On that account, achieving an acceptable level of verification of the extracted data and information is possible.

A wide range of data and pertinent information was extracted and recorded by the authors acting as reviewers of the research articles during the systematic review and meta-analysis. Some of the pertinent information extracted from the research articles include the names of the authors of the research articles and their positions or roles within the

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field of medicine and medical sciences, the ear of publication of the articles, the country, and institutions or health facilities responsible for the research and publication process. On the other hand, some of the data extracted from the chosen research articles include study designs, sample sizes used, the types of ovarian cancer tested, weight and height of the participants, BMI of the participants, treatments and interventions used, outcomes of the treatments and interventions used and conclusions and main findings on the experimental studies that were conducted. The extraction of such pertinent information and data made it possible to realize the effectiveness of the systematic review and meta-analysis in determining the impact BMI has on ovarian cancer.

2.6. Risk of Bias Assessment

A biased assessment of any of the research articles that had met the inclusion criteria by the two independent reviewers was considered the major risk factor for collecting less accurate and credible findings related to the research topic. In this way, the authors of this study undertook two main steps to decrease the risk of a biased assessment during the systematic review and meta-analysis. One such step is that all the articles used for the data extraction process were assessed using the Newcastle-Ottawa Quality Assessment Form for Cohort Studies (NOQAFCS) before synthesizing their findings. That is because most of the research articles used were cohort studies and the participants shared common characteristics such as high or low BMIs and ovarian cancer. Furthermore, there was an assessment of participants' progress to interventions and treatments aimed at managing their BMIs and ovarian cancer over a specific period, such as months or years. The NOQAFCS had scores ranging from 0 to 9 on various factors relating to the quality of research described in the chosen articles, as shown in Table 1 below. Scores were divided into three categories, with articles that scored between 0 and 3 being considered to have low research quality, those between 3 and 6 having moderate research quality, and those between 6 and 9 having a high research quality. The reviewers aimed to ensure that all the articles used for the systematic review and meta-analysis had either a moderate or high research quality. Another step to decrease the risk of biased assessment was solving divergences and contradictions that occurred during the assessment process by an independent and unbiased reviewer. Despite the effectiveness of such steps in decreasing the risk of biased assessment of the articles used in this study, it is estimated that the probability that a biased assessment was incurred is 5%. Since such probability is significantly lower than in many article assessment processes, it is assumable that the current study's findings are very accurate and credible.

2.7. Statistical Analysis

A wide range of statistical analyses was undertaken to prove the validity and accuracy of the research findings based on the statistical tests that were undertaken by the researchers of the articles who established such findings. First, the total effect size that revealed the magnitude of the differences between the randomized controlled trial groups used in the research articles was measured using an odd ratio and correlation coefficient at a 95% Confidence Interval (CI). The Average odd ratio (OR) for the research articles was 0.5, implying that the odds that an outcome in a specific experimental group occurring in another group was half times probable. On the other hand, the average correlation coefficient was 0.64, which implies that there was a positive relationship between the variables of the research articles based on the effect that their independent variables had on their dependent variables. Second, an analysis of the studies' clinical heterogeneity was undertaken using a Cochran Q test and measured using an I^2 statistic. Significant heterogeneity was considered to be an equivalence of I^2 greater than 60% due to the need to obtain accurate and credible research data. In case of significant heterogeneity, a sensitivity analysis was performed. The research articles with a high I^2 statistic were reassessed for various study features such as sample sizes and interventions and treatment efficacy. All the statistical tests used in analyzing the collected data from the research studies were

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two-sided and statistical significance was defined if the p-value, p was less than 0.05. Therefore, in the case of the statistical significance of the p-value, it was assumable that the null hypothesis should be rejected during the interpretation of the collected research data.

2.8. Ethical Considerations

There are two main ethical issues that were considered during the systematic review and meta-analysis. One of them is that the participants who participated in the research studies described in the articles consented to future use of the collected data. In this way, it was not ethically wrong to use their provided data for the purpose of developing more evidence on the current topic of research. Another ethical issue is that the participants involved in the research studies described in the articles expect confidentiality of sensitive data related to their health that may not have been safeguarded during the research study. Resultantly, there was still a need to adhere to the confidentiality of participants' sensitive data as a preservation of their ethical right to use such data for future research studies.

3. Results

3.1. Eligible Studies

Consider chart five below, which shows how the PRISMA guideline was used in the identification of the eligible studies used for the systematic review and meta-analysis. 1030 research articles were obtained from the databases mentioned above using the relevant keywords and phrases. However, 925 of such articles were excluded due to their irrelevance. After screening the remaining articles, 55 were removed since their titles and abstracts were less credible and effective in achieving the research study's purpose. 30 more articles were also excluded during the bias assessment process for having a research quality score of less than 3. Therefore, 20 research studies were considered for the systematic review and meta-analysis, meeting all the inclusion criteria stated in the methodology section above.

3.2. Baseline Characteristics Study

Consider Table 2 below, which shows the baseline characteristics of the research studies used with regard to their nationality of publication. 12 studies were conducted in the United States, while 4 were conducted in the United Kingdom. On the other hand, 2 studies were in Australia, while the remaining two studies were conducted in Canada. All the research studies (n = 20) involved randomized controlled trials, with 15 of them being cohort studies. Population-based cohort studies were (n = 3), while the remaining (n = 2) studies were retrospective cohort studies, as illustrated by Table 3 below. A total of 1,890,100 patients were included in all the studies, whose sample sizes ranged between 2,000 and 189,000 patients. Finally, in all the studies, only female patients were used as the sample participants.

3.3. Risk of Bias

Consider Table 4 below, which shows the risk of bias of the (n=20) research articles that were used for the systematic review and meta-analysis in accordance with their NOQAFCS scores. 15 research studies had a low risk of bias, while 4 were considered to be having a moderate risk. Lastly, only 1 research study had a high risk of bias. Nevertheless, it was still used due to its relevancy to the topic of interest.

3.4. Impact of BMI on Ovarian Cancer

The authors of this study used all the 20 research articles for the systematic review and meta-analysis. The selected studies (n = 20) can be categorized into three groups with regard to the BMI of the participants depending on the synthesized findings that they contained, as illustrated by Table 5 below. They include obesity (BMI>30 kg/m^2),

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Overweight (25<BMI<30 kg/m^2), and normal weight (18<BMI<25 kg/m^2). The findings in all the research articles were related to how BMI impacted ovarian cancer.

3.4.1. Obesity

Ten research studies focused on analyzing how obesity impacted ovarian cancer. All the research studies demonstrated a statistical significance in the relationship between obesity and ovarian cancer with an average p = 0.01. With such an average p-value, the test statistic of the ten research studies was 0.59 standard deviation to the right of the mean on a bell curve. Therefore, Z = 0.59. The odd ratio (OR) of the ten studies was 1.87, which signifies that the likelihood of a similar outcome in the findings of the research articles was 1.87, which is significantly likely. Such OR was based on a confidence interval (CI) of between 0.76 and 1.34. Despite the fact that such research studies had a high OR, the heterogeneity between them was I^2 = 78% which was significantly high. Therefore, the findings of the studies were very dissimilar or diverse based on how they related to the research topic.

3.4.2. Overweight

Eight research studies assessed the effects of being overweight on ovarian cancer. Seven such studies showed statistical significance in the relationship between overweight and ovarian cancer with an average p-value of p = 0.04. The test statistic of the seven research studies was -0.87 standard deviation to the left of the mean on a bell curve, thereby implying the Z = -0.87. The OR of the seven studies was 1.09, signifying that the odds of an outcome in one of them occurring in another was 1.09, which is significantly likely given a CI of between 0.89 and 1.67. Nonetheless, one of the research studies was not statistically significant, given that its p-value was p = 0.09. The heterogeneity between the seven studies that showed statistical significance was I^2 = 67% which was high but not as compared with studies whose main focus was on a sample of participants who were obese. Consequently, there was some level of dissimilarity in the findings of such studies, which led to a synthesis of a diverse number of findings related to the current topic of interest.

3.4.3. Normal Weight

Only two research studies that were included in the systematic review and meta-analysis assessed how normal weight influenced ovarian cancer. Both articles showed that there was no significant difference between having a normal weight and the risk of ovarian cancer. Their average p-value was p = 0.035. The test for the overall effect of the studies revealed that their Z score Z = 1.99 implying 1.99 standard deviations from the mean of their findings with a CI of between 0.97 and 1.54. The OR of the two studies was 0.09, indicating lower odds of exposure among the patients used as a sample to ovarian cancer. Lastly, heterogeneity was I^2 = 62%. Therefore, they also had some dissimilarity in their findings, even though their findings signified that their null hypotheses should be rejected.

4. Discussion

Due to the prevalence of ovarian cancer, many research studies have focused on identifying a wide range of predisposing and precipitating factors that are related to such health conditions. A systematic review and meta-analysis of 20 such research studies were undertaken in this study with the aim of determining the impact that BMI has on ovarian cancer. Half of the research studies used for the systematic review and meta-analysis revealed that there is statistical significance in the relationship between obesity and ovarian cancer with a p-value p = 0.01. Specifically, the researchers of many of such articles were of the notion that obesity which is characterized by BMI greater than 30kg/m^2 has a negative impact on ovarian cancer in those people who are obese are highly likely to experience severe symptoms of ovarian cancer [8] (p.59), [9] (p.539), [10] (p.2230), [11]

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(p.306), [12] (p.1360), [13] (p.559), [14] (p.217), [15] (p.176), [16] (p.35), [17] (p.78). Furthermore, obesity can increase the severity of ovarian cancer, given that it increases the secretion of various sex hormones in females, such as estrogen and progesterone. Due to the accumulation of such sex hormones as adipose tissue around the ovaries, they hasten the process of metastasis, leading to an increased risk of the development of epithelial tumors [6]. In this manner, the studies confirmed the findings of previous research studies that mentioned that being overweight and obese are the second leading causes of ovarian and other cancers [6]. Similar findings were also established by seven research studies whose heterogeneity was I^2 = 67% and p-value of p= 0.04v[13] (p.559), [14] (p.217), [15] (p.176), [16] (p.35), [18] (p.182), [19] (p.30), [20] (p.19), Z = 0.59, CI of between 0.76 and 1.34 and OR of 1.09. Some of the research studies within such a list confirmed that people who are overweight are at a high risk of becoming obese, especially if they develop ovarian cancer. One of the major reasons why such people are at a high risk of developing such type of cancer is because of their likelihood of incurring Liposarcoma, which is a type of cancer that primarily occurs in fat cells [14] (p.217), [15] (p.176), [16] (p.35), [18] (p.182),. Besides, many cancerous cells have been associated with being fueled by the presence of fats or lips in tissues, which promotes their physiological processes and growth, thereby leading to an increase in their level of aggressiveness [14] (p.217), [15] (p.176), [16] (p.35), [18] (p.182),. However, the dissimilarity in the findings (based on their high heterogeneity score of (I^2 = 67%; Z = -0.87; CI = 0.89 to 1.67, p =0.09) of the research articles that analyzed how overweight impacts ovarian cancer was mainly due to the age group of the participants [15] (p.176), [19] (p.30),. Some research studies had younger participants who were at a lower risk of developing ovarian cancer. In comparison, others had older participants who were at a high risk of developing ovarian cancer but at a low risk of being overweight [4] (p.121) [9] (p.539). The main finding of the studies that focused on participants who were overweight was that being overweight resulted in a long-lasting inflammation of tissues and higher than normal insulin levels. Nonetheless, long-lasting inflammation of tissues and higher than normal levels of insulin leads to an increase in the development and growth of cancerous cells due to their promotion of the physiological processes of cancerous cells [4] (p.121) [9] (p.539). The systematic review and meta-analysis showed that very few research studies are focused on determining whether a normal weight can impact the chances of developing ovarian cancer in females. Only two out of the analyzed research articles whose average p-value was 0.035 (statistically significant) and a heterogeneity score of I^2 = 62% [11] (p.306), [21] (p.69), Z score of the studies was 1.99, CI was between 0.97 and 1.54. The finding of the researchers of such articles was that normal weight might not necessarily have an impact on the development of ovarian cancer [11] (p.306), [21] (p.69). Nevertheless, none of the research studies claimed that people who have normal weight have a low risk of developing ovarian cancer [11] (p.306), [21] (p.69). Factors such as lifestyle, use of certain medications, and diet were considered to have the potential to increase the risk of ovarian cancer among such people despite having normal weights [11] (p.306), [21] (p.69). Therefore, some people with normal weight can still develop a such form of cancer while others may not depending on such factors [11] (p.306), [21] (p.69). Therefore, due to the emphasis of many of the research studies on the positive relationship between a high BMI and d risk of developing ovarian cancer and its severe effects, the researchers of the analyzed studies emphasized the need for maintenance of a proper BMI as a strategy of decreasing a person's risk of developing such type of cancer.

5. Conclusions

In conclusion, the proper management of morbidity and mortality resulting from ovarian cancer mandates that there is an implementation of existing clinical evidence obtained from a systematic review and meta-analysis of research studies related to topics that justifies the increase in BMIs of populations as positively related to increased rates of such type of cancer. Therefore, the current study aimed to undertake a systematic review of 23 research studies related to the impact of BMI on ovarian cancer. The research studies

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had to meet a wide range of inclusion criteria being published in English during the past five years before they were screened and assessed for the efficacy of use for academic and research purposes. The findings of the research studies can be categorized into three forms based on the sample of participants of their focus which include obese, overweight, and normal-weight participants. For the research studies which focused on a sample of participants who were obese, Z was 0.59, p = 0.01, OR = 1.87, and CI of between 0.76 and 1.34. The heterogeneity between the studies was I^2 = 78%. The main finding of such research studies was that obesity was positively correlated to a high risk of developing ovarian cancer since it increased the secretion of sex hormones in females. For the research studies which focused on a sample of participants who were overweight, Z = 0.59, CI of between 0.76 and 1.34 and OR of 1.09, and heterogeneity of I^2 = 67%, p = 0.09. The main finding of such research studies was that being overweight contributes to a long-lasting inflammation of tissues and secretion of higher-than-normal levels of insulin, which in turn fuels the process of development and growth of cancerous ovarian cells. Finally, two research studies focused on participants who were normal weight as their sample with a Z score of the studies was 1.99, CI was between 0.97 and 1.54, p = 0.035, and a heterogeneity score of I^2 = 62%. The studies established that normal weight does not necessarily contribute to ovarian cancer even though people who have a normal weight cannot be considered to be at low risk of experiencing such type of cancer. Therefore, from a systematic review and meta-analysis of the studies, it is evident that populations need to properly manage their BMIs to reduce their risk of various forms of cancer, including ovarian cancer. However, future research studies should assess whether a decrease in the BMI of patients with ovarian cancer is necessary to improve the effectiveness of treatments and interventions for such types of cancer. Furthermore, future studies should determine why some people with high BMIs may be at more risk of other types of cancer other than ovarian cancer.

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Appendices

Table 1. Research Quality Scores of the Studies Used in Accordance with NOQAFCS.

Research Quality Score	Research Articles
Between 0 and 3	Shabir & Gill, 2020.
Between 3 and 6	Aarestrup et al., 2019. Avgerinos et al., 2019. Huang et al., 2022. Kim et al., 2020.
Between 6 and 9	Alizadeh et al., 2019. Arthur et al., 2018. Bauersfeld et al., 2018. Chu et al., 2018. Fortner et al., 2019. Huang et al., 2020. Huang et al., 2019. Huang et al., 2018. Lee & Lee, 2020. Mizushima & Miyamoto, 2019. Nash & Menon, 2020. Perry & Shulman, 2020. Qian et al., 2019. Rinninella et al., 2020. Yao et al., 2019.

Table 2. Baseline characteristics of the research studies used with regard to their nationality of publication.

Nationality of Publication	Research Articles
United States	Huang et al., 2020. Huang et al., 2019. Huang et al., 2018. Aarestrup et al., 2019. Avgerinos et al., 2019. Huang et al., 2022. Kim et al., 2020. Perry & Shulman, 2020. Mizushima & Miyamoto, 2019. Bauersfeld et al., 2018. Alizadeh et al., 2019 Shabir & Gill, 2020.
United Kingdom	Chu et al., 2018. Nash & Menon, 2020. Yao et al., 2019. Fortner et al., 2019.
Australia	Lee & Lee, 2020.

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	Rinninella et al., 2020.
Canada	Arthur et al., 2018. Qian et al., 2019.

Table 3. Nature of the Research Studies

Nature of the Study	Research Articles
Cohort study	Aarestrup et al., 2019. Shabir & Gill, 2020. Fortner et al., 2019. Huang et al., 2020. Huang et al., 2022 Huang et al., 2019. Huang et al., 2018. Kim et al., 2020 Lee & Lee, 2020. Mizushima & Miyamoto, 2019. Nash & Menon 2020. Perry & Shulman 2020. Rinninella et al., 2020. Yao et al., 2019. Avgerinos et al., 2019.
Population-based cohort study	Qian et al., 2019. Bauersfeld et al., 2018. Chu et al., 2018.
Retrospective cohort study	Alizadeh et al., 2019. Arthur et al., 2018.

Table 4. Risk of Bias of the Research Articles

Risk of Biasness	Research Articles
High	Shabir & Gill, 2020.
Moderate	Aarestrup et al., 2019. Avgerinos et al., 2019. Huang et al., 2022. Kim et al., 2020.
Low	Alizadeh et al., 2019. Arthur et al., 2018. Bauersfeld et al., 2018. Chu et al., 2018. Fortner et al., 2019.

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	Huang et al., 2020. Huang et al., 2019. Huang et al., 2018. Lee & Lee, 2020. Mizushima & Miyamoto, 2019. Nash & Menon, 2020. Perry & Shulman, 2020. Qian et al., 2019. Rinninella et al., 2020. Yao et al., 2019.

Table 5. BMI Group of Focus of the Research Articles.

BMI Group of Focus	Research Studies
Obesity	Fortner et al., 2019. Huang et al., 2020. Huang et al., 2022 Huang et al., 2019. Huang et al., 2018. Kim et al., 2020 Lee & Lee, 2020. Mizushima & Miyamoto, 2019. Nash & Menon 2020. Perry & Shulman 2020.
Overweight	Alizadeh et al., 2019. Arthur et al., 2018. Bauersfeld et al., 2018. Chu et al., 2018. Qian et al., 2019. Rinninella et al., 2020. Yao et al., 2019. Avgerinos et al., 2019.
Normal weight	Aarestrup et al., 2019. Shabir & Gill, 2020.

Table 6. Summary of the Research Articles Used for the Systematic Review and Meta-Analysis

Author and Year	Research Design	Outcomes of Measures	Findings
Aarestrup et al., 2019	Cohort study	Weight, BMI, Height	People who are of normal weight are still at risk of developing ovarian cancer but at a lower rate than overweight and obese individuals.

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Alizadeh et al., 2019	Retrospective cohort study	Weight, BMI, Height	Being overweight increases the risk of the development and growth of cancerous ovarian cells.
Arthur et al., 2018	Retrospective cohort study	Weight, BMI, Height	Being overweight is associated with a high risk of developing ovarian cancer
Avgerinos et al., 2019	Cohort study	Weight, BMI, Height	Being overweight fosters the inflammation of tissues which worsens ovarian cancer.
Bauersfeld et al., 2018	Population-based cohort study	BMI	Being overweight promotes the secretion of higher-than-normal insulin levels, thereby enhancing the growth of cancerous ovarian cells.
Chu et al., 2018	Population-based cohort study	BMI	Being overweight is associated with severe health effects of ovarian cancer.
Fortner et al., 2019	Cohort study	BMI	Obesity leads to increased ovarian cancer risk
Huang et al., 2020	Cohort study	Weight, BMI, Height	Obesity can increase the risk of developing ovarian cancer
Huang et al., 2019	Cohort study	BMI	Obesity is positively correlated to a high risk of ovarian cancer
Huang et al., 2018	Cohort study	Weight, BMI, Height	Obesity is positively correlated to a high risk of ovarian cancer
Huang et al., 2022	Cohort study	Weight, BMI, Height	Obesity is positively correlated to a high risk of ovarian cancer
Kim et al., 2020	Cohort study	Weight, BMI, Height	Managing obesity can reduce ovarian cancer risk.
Lee & Lee, 2020	Cohort study	Weight, Height	Ovarian cancer symptoms are worse in obese people.
Mishuzima & Miyamoto, 2019	Cohort study	Weight, BMI, Height	Obesity can promote the severity and rapid growth of cancerous ovarian cells
Nash & Menon, 2020	Cohort study	Weight, BMI, Height	Obesity increases the risk of developing ovarian cancer
Perry & Shulman, 2020	Cohort study	Weight, BMI, Height	Managing obesity can be effective in reducing the risk of ovarian cancer.
Qian et al., 2019	Population-based cohort	Weight, Height	Being overweight leads to an increased risk of developing ovarian cancer.
Rinninella et al., 2020	Cohort study	Weight, BMI, Height	A positive correlation exists between being overweight and a high risk of developing ovarian cancer.
Shabir & Gill, 2020	Cohort study	Weight, Height	People with normal weight are at a lower risk of developing ovarian cancer than obese and overweight individuals.
Yao et al., 2019	Cohort study	Weight, BMI, Height	Being overweight fuels the growth and development of cancerous ovarian cells.

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Table 7. A Meta-Analysis Forest Plot of the Included Research studies

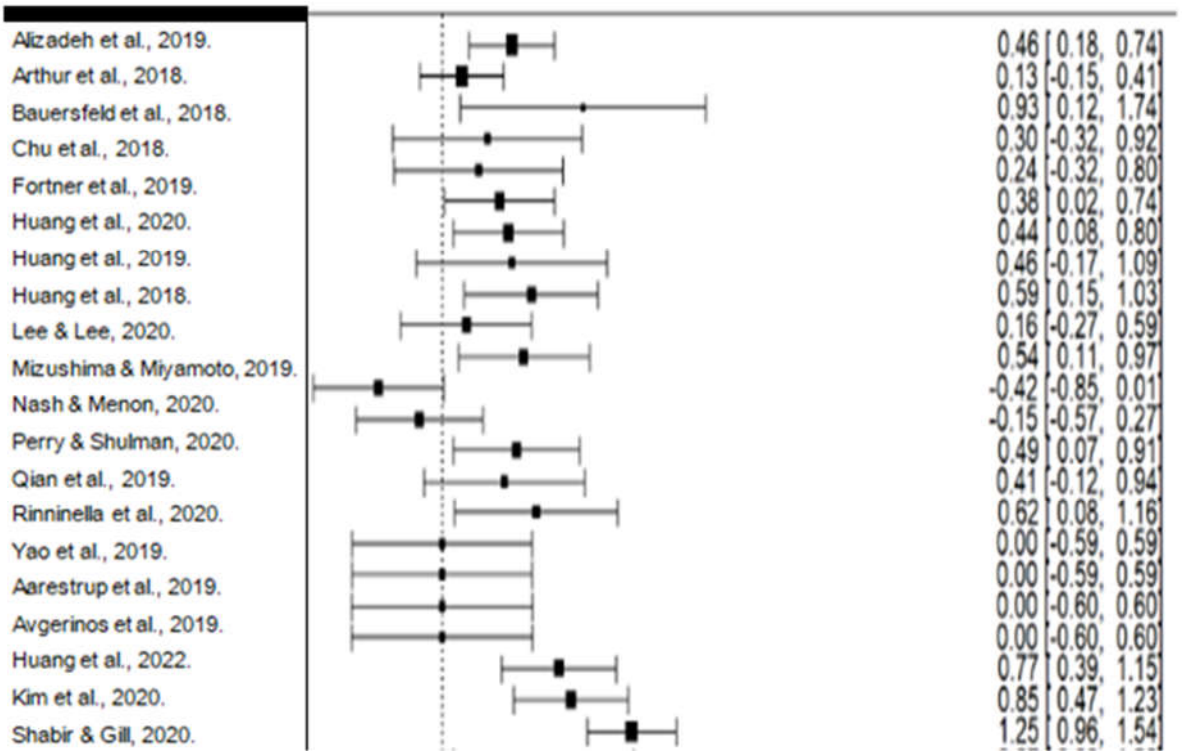
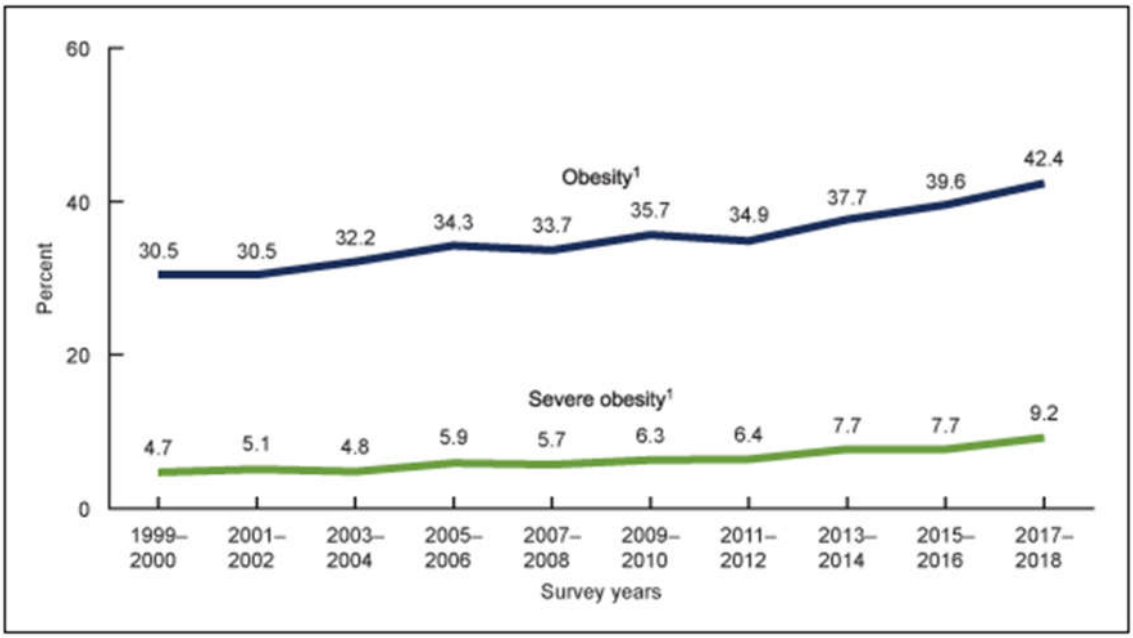


Chart 1. Obesity Trends in the United States



Source: (Center for Disease Control, 2022)

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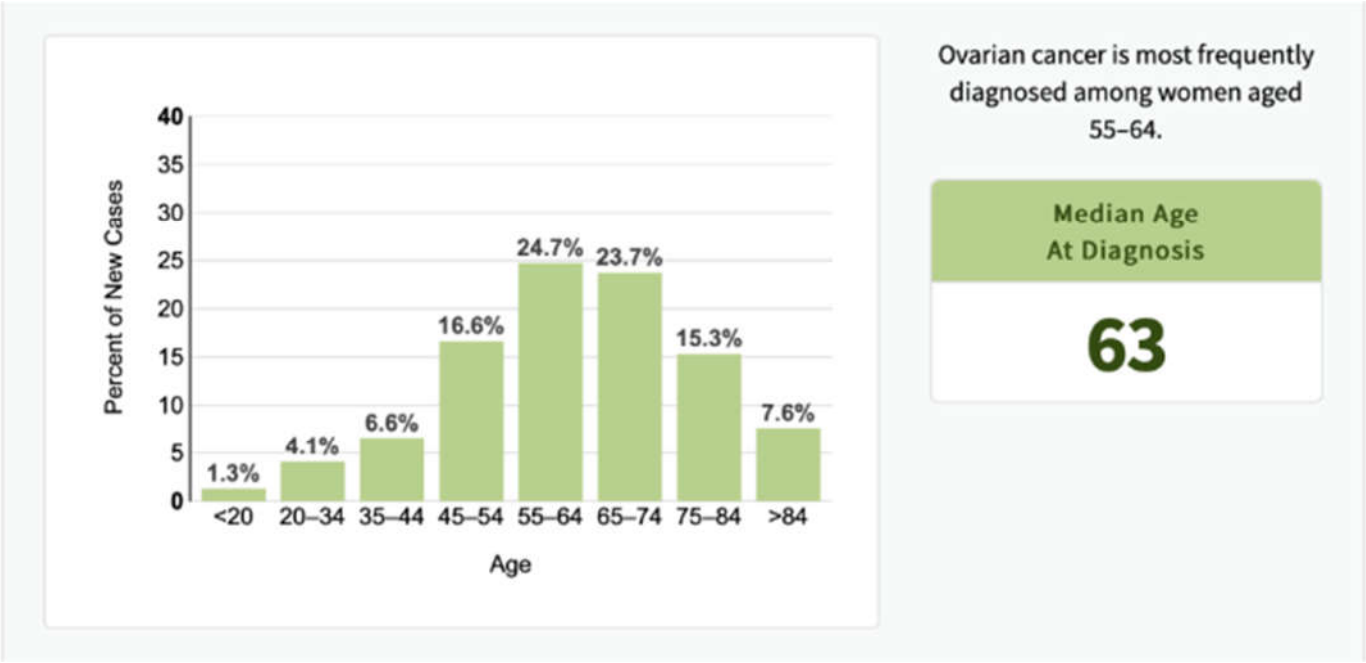
Chart 2. Ovarian Cancer Trends in the United States



Source: (Center for Disease Control, 2022)

Chart 3. PRISMA flow Chart

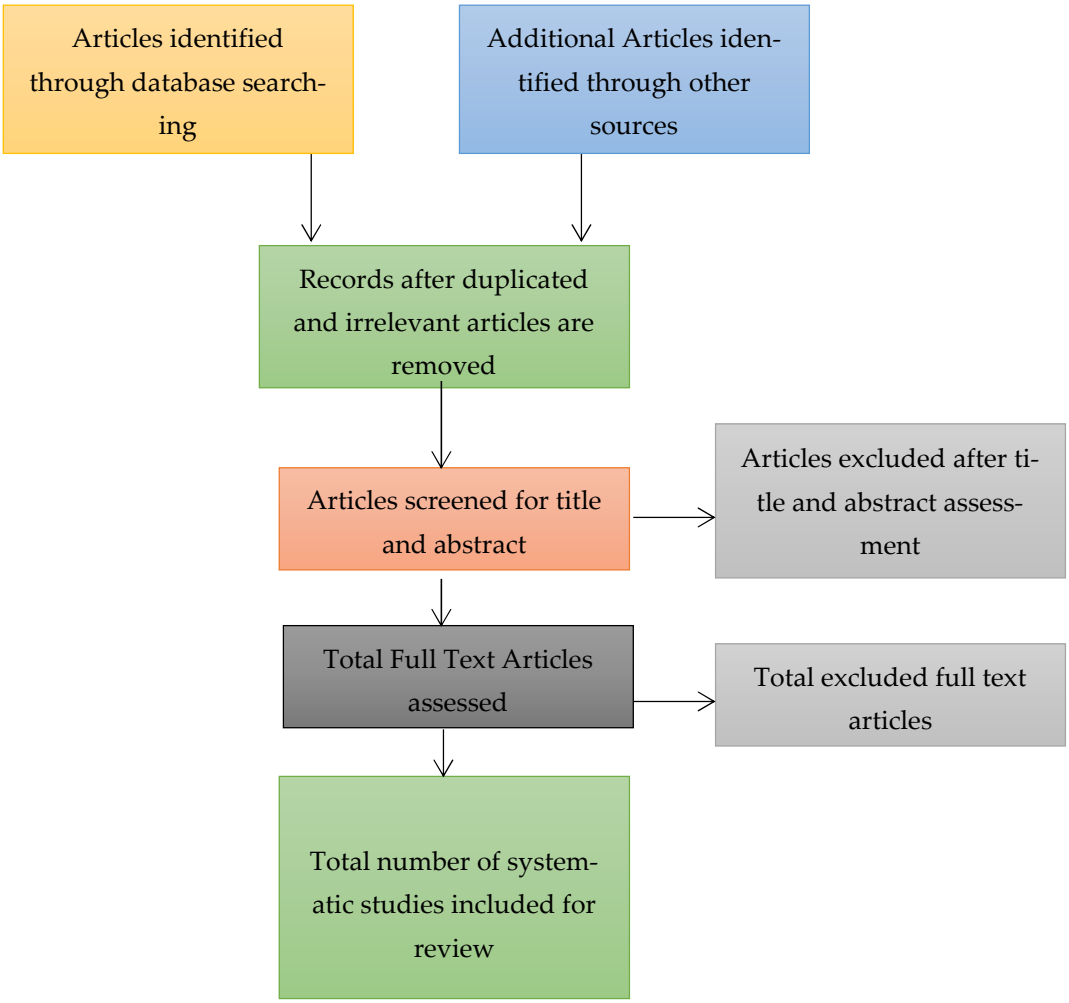


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Chart 4. Databases Used in Identifying the Research Articles

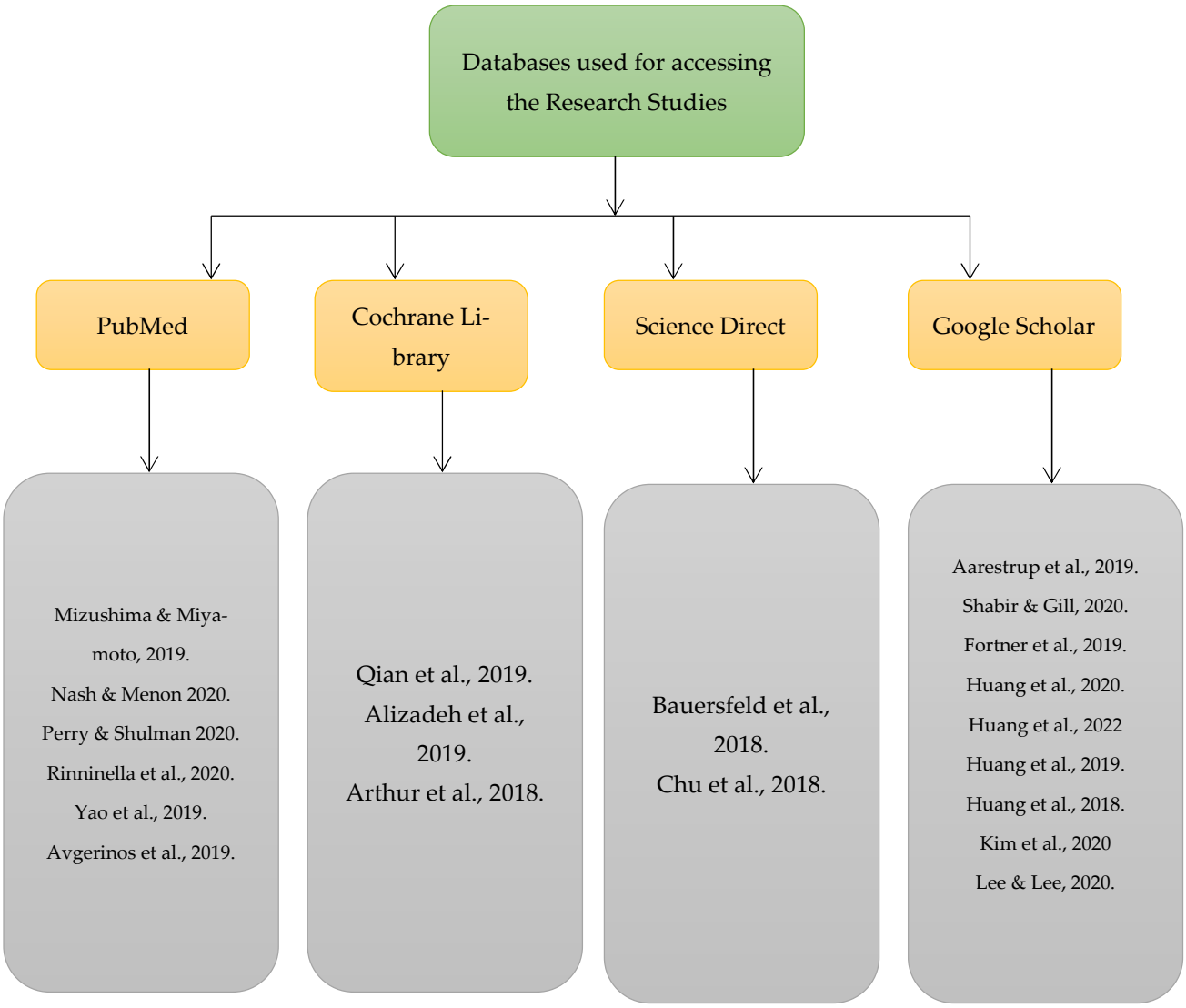

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Chart 5. Inclusion and exclusion of the Research Articles based on the PRISMA flow Chart