

# Cancer risks in patients with obesity and metabolic syndrome: integrative analysis of studies published between 2020 and 2024

## Riscos de câncer em pacientes com obesidade e síndrome metabólica: análise integrativa de estudos publicados entre 2020 e 2024

## Riesgos de cáncer en pacientes con obesidad y síndrome metabólico: análisis integrativo de estudios publicados entre 2020 y 2024

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**Como citar:** Santos MTKF, Santos ICP, Jorge IN, Aleixo GVF, Huck L, Filho ES. Cancer risks in patients with obesity and metabolic syndrome: integrative analysis of studies published between 2020 and 2024. REVISA. 2026; 15(Esp.4): 27-33. Doi: <https://doi.org/10.36239/revisa.v15.nEsp4.p27-33>

# REVISA

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Recebido 27/01/2026  
Aprovado: 22/03/2026

### RESUMO

**Objetivo:** A obesidade e a síndrome metabólica configuram importantes fatores de risco modificáveis para o câncer. Esta revisão integrativa incluiu cinco meta-análises publicadas entre 2020 e 2024, identificadas nas bases PubMed e BVS. Os resultados demonstraram associação consistente entre obesidade, síndrome metabólica e maior risco de neoplasias, especialmente câncer colorretal, endometrial, hepático, pancreático, vesical e mamário na pós-menopausa. Os mecanismos envolvidos incluem inflamação crônica, resistência insulínica, alterações hormonais e disfunções metabólicas. Conclui-se que a avaliação metabólica deve ser incorporada às estratégias de prevenção e manejo clínico do câncer, reforçando a importância do controle da obesidade no enfrentamento das doenças crônicas não transmissíveis.

**Palavras-chave:** Doenças Crônicas Não Transmissíveis; Alterações hormonais; Inflamação Crônica; Oncologia.

### ABSTRACT

**Objective:** Obesity and metabolic syndrome are important modifiable risk factors for cancer. This integrative review included five meta-analyses published between 2020 and 2024, identified in the PubMed and BVS databases. The results demonstrated a consistent association between obesity, metabolic syndrome, and an increased risk of neoplasms, especially colorectal, endometrial, liver, pancreatic, bladder, and breast cancer in postmenopausal women. The mechanisms involved include chronic inflammation, insulin resistance, hormonal changes, and metabolic dysfunctions. The conclusion is that metabolic assessment should be incorporated into cancer prevention and clinical management strategies, reinforcing the importance of obesity control in combating chronic noncommunicable diseases.

**Keywords:** Chronic Noncommunicable Diseases; Hormonal Changes; Chronic Inflammation; Oncology.

### RESUMEN

**Objetivo:** La obesidad y el síndrome metabólico son importantes factores de riesgo modificables para el cáncer. Esta revisión integrativa incluyó cinco metanálisis publicados entre 2020 y 2024, identificados en las bases de datos PubMed y BVS. Los resultados demostraron una asociación consistente entre la obesidad, el síndrome metabólico y un mayor riesgo de neoplasias, especialmente cáncer colorrectal, de endometrio, de hígado, de páncreas, de vejiga y de mama en mujeres posmenopáusicas. Los mecanismos implicados incluyen inflamación crónica, resistencia a la insulina, cambios hormonales y disfunciones metabólicas. La conclusión es que la evaluación metabólica debe incorporarse en las estrategias de prevención y manejo clínico del cáncer, lo que refuerza la importancia del control de la obesidad en la lucha contra las enfermedades crónicas no transmisibles.

**Palabras clave:** Enfermedades crónicas no transmisibles; Cambios hormonales; Inflamación crónica; Oncología.

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## Introduction

Obesity and metabolic syndrome emerge as modifiable risk factors for several chronic noncommunicable diseases, including cancer, one of the main causes of morbidity and mortality worldwide.<sup>1-2</sup> In Brazil, obesity affects approximately 31% of adults,<sup>3</sup> and about 25% of the world's population suffers from metabolic syndrome (MetS).<sup>4</sup>

Cancer, the second leading cause of death in Brazil, presents more than 600,000 new annual cases.<sup>5</sup> Growing evidence demonstrates that obesity and metabolic syndrome increase the risk of neoplasms, especially postmenopausal breast, colon and rectum, kidney, liver, and pancreas cancer.<sup>6-7</sup>

The pathophysiological mechanisms underlying this relationship are multiple and interdependent. Obesity is associated with a state of low-grade chronic inflammation, insulin resistance, hyperinsulinemia, and changes in the production of adipokines and sex hormones, creating an environment favorable to carcinogenesis.<sup>8</sup> Metabolic syndrome, which includes central obesity, arterial hypertension, dyslipidemia, and glucose intolerance, potentiates these processes through common metabolic and inflammatory pathways, demonstrating the oncological risk.<sup>9</sup>

Given the magnitude of the problem and its clinical and epidemiological relevance, it is fundamental to comprehensively understand the association between obesity, metabolic syndrome, and cancer risk. This understanding allows not only for the identification of populations with greater vulnerability but also for guiding more effective prevention, screening, and clinical management strategies.<sup>1,7</sup>

Thus, the present study aimed to analyze the relationship between obesity and metabolic syndrome and the risk of developing cancer, highlighting the most frequently associated types.

## Method

This is an integrative literature review on the association between obesity, metabolic syndrome, and cancer risk. The search was conducted in the PubMed/MEDLINE (National Library of Medicine, USA) and Virtual Health Library (BVS) databases, using controlled descriptors (MeSH) and free terms in English and Portuguese, combined with Boolean operators. Only meta-analysis articles, published between 2020 and 2024, available in free full text, and with an adult population, were included.

In PubMed/MEDLINE, the strategy used was: ("Obesity"[MeSH]) AND ("Neoplasms"[MeSH] OR cancer OR oncogenesis OR tumor) and ("Metabolic Syndrome"[MeSH]) AND ("Neoplasms"[MeSH] OR cancer OR oncogenesis OR tumor). In BVS, the strategy used was: ("síndrome metabólica" OR "metabolic syndrome") AND (câncer OR cancer OR neoplasia OR tumor OR oncogênese) AND (adulto OR adult) and (obesidade OR obesity) AND (câncer OR cancer OR neoplasia OR tumor OR oncogênese) AND (adulto OR adult).

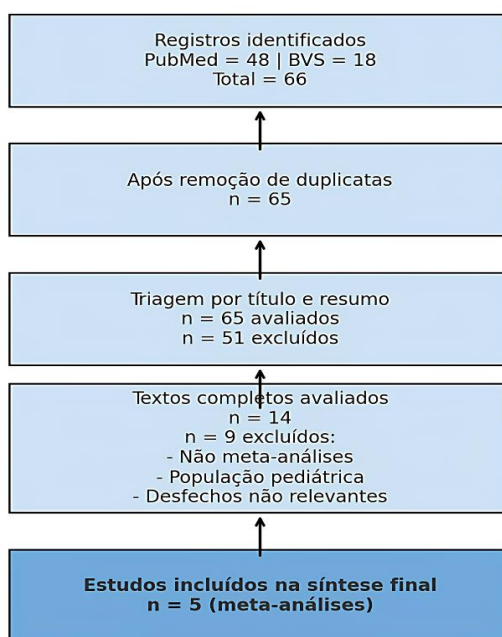
Exclusion criteria included pediatric studies, systematic reviews without meta-analysis, preclinical or animal trials, case reports, editorials, letters to the editor, dissertations, theses, and articles that did not present results directly related to the investigated association.

The selection of articles occurred in three stages: (1) screening by title and abstract, (2) full reading to confirm eligibility, and (3) organization of studies in a standardized spreadsheet, with extraction of information on authors, year, country, methodological design, studied population, and the type of cancer evaluated.

## Results

66 records were identified (PubMed = 48; BVS = 18). After exclusions, 5 meta-analyses met the eligibility criteria and were included in the synthesis (Figure 1).

**Fluxograma PRISMA - Seleção dos estudos (2020-2024)**



**Figure 1** - PRISMA flowchart of study selection (2020-2024).

**source:** Elaborated from the data of the integrative review (PubMed and BVS).

The main methodological characteristics and the findings of each included study are systematized in Table I.

**Table I** - Description of the studies included in the integrative review on obesity, metabolic syndrome associated with cancer risk (2020-2024).

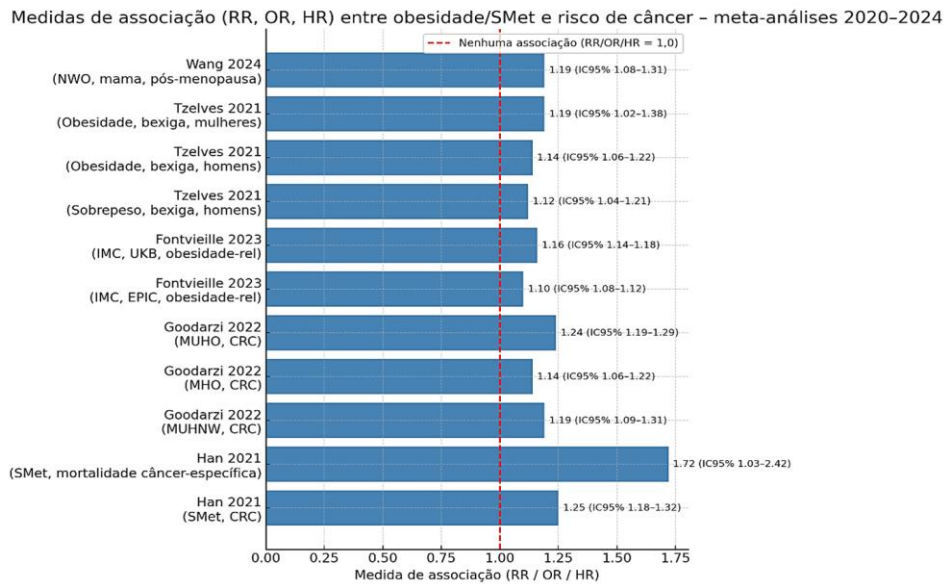
Author/Year	Country/Region	Study Type	Population/Sample	Evaluated Exposure	Type of Cancer/Outcome
Han et al., 2021	Ásia, Europa, EUA	Meta-analysis	30 studies	Metabolic syndrome	Colorectal cancer

	s					
Goodarzi et al., 2022	USA, Korea	UK,	Meta-analyses	759.066	Metabolic phenotypes (obesity and MetS)	Colorectal cancer
Fontvieille et al., 2023	Europe, UK		Meta-analyses	577.343	Obesity (BMI)	13 Obesity-related cancers
Tzelves et al., 2021	Europe, Canada, Australia	USA, Asia,	Meta-analyses	49.647.098	Obesity	Bladder cancer
Wang et al., 2024	UK		Meta-analyses	74.763	Obesity	Postmenopausal breast cancer

**Source:** Elaborated from the studies included in the integrative review.<sup>11-15</sup>

Among the included studies, it was observed that metabolic syndrome was associated with an approximate 25% increase in the risk of colorectal cancer.<sup>11</sup> Similarly, Goodarzi et al. evidenced that adverse metabolic phenotypes, even in individuals of normal weight, significantly increased the risk of colorectal cancer.<sup>12</sup> Fontvieille et al. demonstrated that increments in body mass index were associated with a 10% to 16% higher risk of different obesity-related cancers.<sup>13</sup> Tzelves et al. identified that both overweight and obesity elevated the risk of bladder cancer, especially in men, and that central obesity also represented an important risk factor.<sup>14</sup> Finally, Wang et al. showed that women with normal weight obesity presented a higher risk of postmenopausal breast cancer.<sup>15</sup>

Figure 2 presents the graphical comparison of the association measures of the included studies. All works identified values above the reference line (RR/OR/HR = 1.0), indicating an **increased risk of cancer** in different contexts of obesity and metabolic syndrome. Each bar represents the point measure of the relative risk (RR), odds ratio (OR), or hazard ratio (HR) according to the type of exposure evaluated (metabolic syndrome, BMI = body mass index, metabolic phenotypes, normal weight obesity, or central obesity) and the type of cancer. The horizontal bars indicate the 95% confidence intervals (CI95%). The red dashed line represents no association (reference value = 1.0).



**Figure 2** Forest plot of association measures between obesity, metabolic syndrome, and cancer risk, meta-analyses 2020–2024. **Source:** Elaborated from the studies included in the integrative review.<sup>11-15</sup>

**Abbreviations:** CRC = colorectal cancer; MHNW = metabolically healthy normal weight; MUHNW = metabolically unhealthy normal weight; MHO = metabolically healthy obese; MUHO = metabolically unhealthy obese; NWO = normal weight obesity.;

## Discussion

The findings corroborate the literature by identifying consistent associations between obesity, metabolic syndrome, and certain types of cancer, especially postmenopausal breast, colorectal, endometrial, liver, and pancreatic cancer, which reinforces the role of adiposity and metabolic dysfunctions in carcinogenesis.<sup>16-14</sup> Similar patterns, mainly for colorectal and endometrial cancer, stand out as the most associated.<sup>18-19</sup>

Low-grade chronic inflammation and insulin resistance emerge as central pathways in this relationship. Dysfunctional adipose tissue releases pro-inflammatory cytokines, such as TNF-alpha and IL-6, which stimulate cell proliferation and tumor angiogenesis.<sup>20</sup> Furthermore, hyperinsulinemia associated with metabolic syndrome increases circulating IGF-1 levels, favoring proliferative signaling and inhibition of apoptosis. This mechanism was also described in cohort population analyses by Anderson et al., suggesting consistency between different populations.<sup>21</sup>

Although the association between obesity and postmenopausal breast cancer is consistent, some studies point to divergent results in premenopausal women, suggesting the influence of modifying factors.<sup>16-18</sup>

Regarding the types of cancer identified in this review, some pathophysiological justifications are particularly relevant. In the case of the endometrium, hyperestrogenism resulting from peripheral aromatization in adipose

tissue constitutes a key mechanism in tumor promotion. In colorectal cancer, intestinal dysbiosis and the chronic inflammatory state appear to play a determining role.<sup>19</sup>

## Final Considerations

Obesity and metabolic syndrome play a significant role in carcinogenesis, especially in colorectal, endometrial, liver, pancreatic, and postmenopausal breast cancers. However, divergences persist regarding other tumors, such as prostate and breast cancer in premenopausal women, which highlights areas of knowledge to be unveiled and the need for further investigations. This study reinforces the importance of incorporating metabolic assessment into prevention strategies and clinical practice, recognizing the fight against obesity as a strategic component in combating chronic noncommunicable diseases.

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