# Effect of cannabis and subproducts on anthropometric measures: a systematic review and meta-analysis

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REVIEW ARTICLE

Epidemiology and Population Health

# Effect of cannabis and subproducts on anthropometric measures: a systematic review and meta-analysis

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**BACKGROUND:** Obesity poses a significant public health challenge. Research has examined the impact of cannabis and subproducts on health but varying results have hindered a consensus.
**AIM:** This study aimed to evaluated the effects of cannabis and subproducts on body measurements.
**METHODS:** For searching randomized controlled trials evaluating cannabis and/or subproducts use and changes in anthropometric measures, a systematic search at MEDLINE, Embase, Cochrane Library and Web of Science was conducted until March 2023. The outcomes included changes in body weight, body mass index (BMI) and waist circumference (WC). Meta-analysis was realized using R software (version 4.2.1).
**RESULTS:** In general, cannabis use reduced weight by 1.87 kg (95% CI: −3.71 to −0.03) and WC (mean difference = −2.19, 95% CI: −4.44 to 0.06). When examining subgroups, longer follow-up periods were associated with a more pronounced BMI reduction (mean difference = −1.10, 95% CI: −2.23 to 0.03). Cannabinoid CB1 exhibited an increase in body fat (mean difference = 1.70, 95% CI: 0.66–2.74).
**CONCLUSION:** These findings suggest that cannabis and subproducts could be considered adjuncts in obesity treatment by helping to reduce relevant anthropometric measurements.

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## INTRODUCTION

Obesity is a significant public health issue around the world [1]. It is predicted that it currently attracts 650 million adults [2] and by 2025, this number will rise by 50 million [3]. This condition results in countless metaphysical changes as well as severe and chronic diseases that lower life expectancy [4]. Part of the complications associated with obesity are linked to an excess of body fat, which is a highly inflammatory condition and disrupts the symbiotic functioning of the body, leading to a variety of cardiac, cerebral, vascular, skeletal, and hemodynamic malfunctions and the establishment of critical morbidity quadrangles (Fig. 1) [5].

Various strategies including improvements to the standards for physical activity [6], and the adoption of healthier eating guidelines, as well as some medication-related interventions [7] (such as orlistat and sibutramina) and surgical interventions, such as the bandage laparoscopic, Bypass Gastric, Duodenal Switch, Gastrectomy Vertical (Sleeve) [8] among others, suggestions which have been made to reduce the body's indicative measurements of fat mass and, as a result, obesity [4].

The use of *Cannabis sativa* to treat and relieve the symptoms of some diseases has increased in recent years, being applied in the treatment of various neuropsychiatric, gastrointestinal, or pain situations. However, secondly, although its use has shown good tolerance for some diseases, adverse effects have also been shown to be frequent in relation to psychiatric disorders (mood disorders, anxiety) among other symptoms when used in the long term [9]. In addition, the endocannabinoid system's receptors are found in many different parts of the body, primarily the brain and central nervous system [10], which has an impact on a variety of physiological processes. These parts of the body include the stomach, muscle, pancreas, and adipose tissue. Studies in progress [11–13] have suggested a connection between the endocannabinoid system and this serious global disease [14]. Given that obesity and bodily inflammation are linked, the endocannabinoid system may act in conjunction with cannabis use as a treatment for metabolic imbalances.

The current body of literature has produced numerous studies linking numerous diseases to cannabis use, whether for therapeutic or recreational purposes. Determining the benefits [15, 16] and drawbacks [17] of its use, numerous discoveries have been made in recent years in this manner; however, the effects of cannabis and its derivatives when used alone are still not fully understood [18]. In order to assess additional studies and gain a deeper understanding of the topic and to ensure scientific

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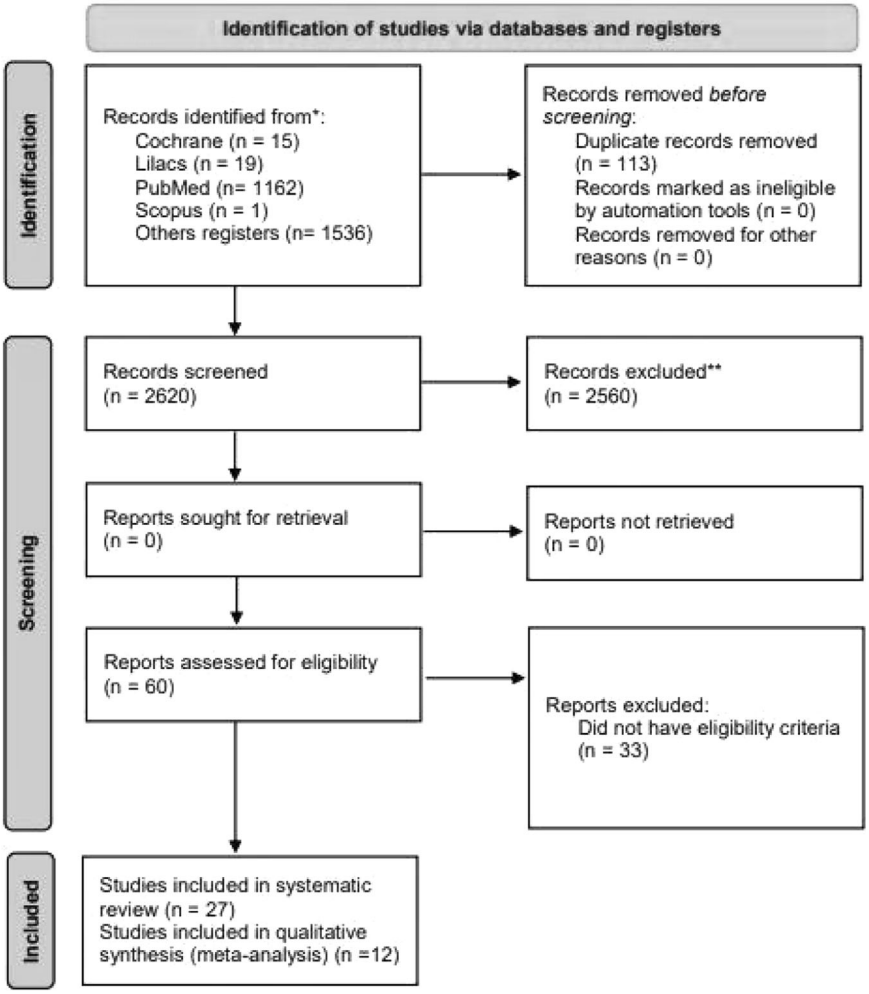


**Fig. 1 Flowchart for the selection of studies, 2023.** *Electronic databases; **records excluded in title and abstract analysis.

credibility, this aim review evaluates the the effect of cannabis and subproducts on anthropometric measures changes.

## METHODS

This systematic review and meta-analysis followed the recommendations of the Cochrane Guidelines for Systematic Reviews of Interventions [19] and was developed according to PRISMA [20]. The study's protocol was registered on the PROSPERO platform under code CRD42023399615.

### Search strategy and selection criteria

We searched the independent databases MEDLINE (PubMed), EMBASE, Cochrane Library (Central), and Web of Science to identify randomized controlled trials (RCTs) evaluating the use of cannabis and subproducts as modifying agents of anthropometric changes related to obesity in adults. Additionally, selected study references were evaluated by hand search.

The descriptors were found in the Medical Subject Headings (MeSH), the Health Sciences Descriptors (DeCS), and the EMBASE Subject Descriptors (Emtree) databases. There were no language, date, document type, or publication status restrictions on the inclusion of registers. The search in literature was done up to March 10th, 2023. The search strategy was modified based on the descriptions of each database, and it is presented in Appendix A.

The inclusion criteria took into account intervention studies that assessed changes in indicators and obesity indices related to adults with the use of cannabis and subproducts. Studies without the use of cannabis and subproducts as a therapeutic agent, studies involving individuals under the age 18, studies using animals, various types of reviews (narrative, integrative, systematic with and without meta-analysis), studies conducted in vitro, editorials, protocols without results, and studies that did not evaluate the study's primary endpoints (obesity indicators and indices), were all considered criteria for exclusion.

The use of cannabis and subproducts or its derivatives as a therapeutic agent was defined as intervention (i.e., rimonabant, taranabant, hemp oil). The outcomes included changes in body fat percentage: weight, body mass index (BMI), waist circumference (WC) as well as the secondarily reduced mass of fat, measured by the dual-energy absorption (DXA).

## DATA EXTRACTION AND QUALITY ASSESSMENT

We uploaded the electronic search results from the defined databases to the Rayyan Qatar Computing Research Institute app for systematic reviews [21].

Two reviewers (DT e MR) independently screened titles and abstracts. These reviewers independently assessed each eligible study to determine whether they met the inclusion criteria. A third independent reviewer (NSG) addressed any discrepancy. To create the extraction table, the following information was collected: reference, title, journal, country, design study, time of follow-up (days), baseline characteristics, cannabis and subproducts dosage,

age and sex, results (changes in obesity indicators and indices), and data collection methods (DXA, anthropometry, and bio impedance), limitations of the study, and key findings.

Our Joanna Briggs Institute (JBI) critical appraisal tool is used to evaluate the risk of bias in randomized controlled trials [22]. Two researchers independently assessed the risk of bias in the chosen studies. Disagreements among the reviewers regarding the potential for bias in particular studies will be settled through discussion, occasionally involving a third author of the review. The Supporting material 02 presents the criteria and considerations made by the reviewers in response to the inquiries from the JBI's revised critical assessment tool for RCTs.

In order to better comprehend and contextualize the effect of cannabis and subproducts use on changes in body composition, the delta (Δ) was employed to measure the difference in means found in each subgroup, at the beginning (baseline) and at the end (follow-up) of the data collection, through the calculation of $\Delta_{Total=\Delta_{follow-up}-\Delta_{baseline}}$ [23]. Additionally, to understand the variability using standard deviations ($\sigma$), the formula was utilized $\sigma = \sqrt{\frac{\sigma_1^2}{N_1} + \frac{\sigma_2^2}{N_2}}$, where 1 represents the baseline and 2 represents the follow-up.

## META-ANALYSIS

In order to take into account, the differences between the studies, a meta-analysis using the random-effects model was conducted for the combinable studies [24, 25]. The purpose of the meta-analysis was to evaluate the relationship between cannabis use and changes in the anthropometric indicators or indices of young adults and adults. The studies' heterogeneity and consistency will be evaluated using the Cochran Q-test and quantified using the $I^2$ test [20–26].

The total treatment effects were visualized using forest plots. The visual funnel plot inspection and Egger test calculation will be used to evaluate the publication preview [27]. Subgroup analyses were performed using cannabis and subproducts type and studies time follow-up. All analyses will be carried out on R software, version 4.2.1, using the 'Meta' packages, versions 6.0-0.

## RESULTS

Searches for information produced 2620 articles. Out of those 113 were duplicates, and 2560 were eliminated from consideration after reading the titles and summaries. In the textual analysis stage, 60 articles were carefully evaluated. From these, 33 were eliminated, and the remaining candidates were chosen and included in systemic analyses ($N = 27$). Twelve of which were also included in the meta-analyses, displays the selection flowchat process (Fig. 1) (Supplementary Material 01).

The studies that were published between 2005 and 2022 included 12 RCT (44%) (Table 1). A total of 4394 participants were included with 2674 in the intervention group and 1720 in the control group. Participants' ages ranged from 18 to 70 years old. The included studies had follow-up lasting between 42 [27] and 1338 days [28].

In the articles assessed for the systematic review and meta-analysis, 92.6% ($N = 25$) of case-control studies were used, and only 7.4% ($N = 2$) of cohort studies were included. The majority of studies were conducted in the United States ($N = 7$; 58%), followed by the United Kingdom ($N = 3$; 25%), Finland and France ($N = 2$ in each country; 16%), and Canada, Portugal, Argentina, Iran, Sweden, Switzerland, Holland, and Spain ($N = 1$ in each country; 8%). The cannabis and subproducts used in the studies included were Rimonabant (8 studies) [29–36]; Δ9-Tetrahidrocanabinol (THC) and analogies (2 studies) [37, 38]; cannabidiol (1 study) [37], β-caryophyllene (1 study) [36] and hemp oil (1 study) [27].

In which the dosage varied according to the medication, Rimonabant 5 mg was offered in 22.2% of the studies ($N = 6$), Rimonabant 20 mg in 29.6% of the studies ($N = 18$), Taranabant 0.5 and 1 mg in 11.1% of the studies ($N = 3$ studies each), Taranabant 2 mg in 14.8% of the studies ($N = 4$), Taranabant 4 and 6 mg, as well as Dronabinol 2.5 mg and 10 mg, were offered in 3.7% of the studies ($N = 1$ study each). It is worth noting that specific dosages for CBD, THCV, hemp oil, and β-caryophyllene were not reported.

All studies were evaluated based on measurements of body weight, BMI, and body fat, allowing each study to use a unique type of cannabis and subproducts that would have an impact on both subjects. In addition, the studies considered in this systematic and meta-analysis produced findings that could support the reasons why we chose to investigate the relationship between cannabis use and obesity. As a result, significant findings from this study, such as the reduction of WC and increase in body mass, as well as those without statistical significance related to the BMI among other variables, such as the length of the study and the number of participants, depending on the type of cannabis and subproducts used, allowed discussion about the reasons why science still has conflicting hypotheses about the use of cannabis and subproducts as modifying agents of anthropometric changes related to obesity.

We describe the studies that were used in the meta-analysis in Table 1 so that additional characteristics, such as primary goals and secondary outcomes, can be seen in the supplemental material. Also, the main results found from the meta-analysis are presented in Table 2, and more results the analysis of subgroups was described in supplementary material.

From the comparative analysis of each group, it was possible to see that the effects of cannabinoid use on weight and WC reduction were on a larger scale. There was a decrease of 1.87 kg in weight (mean difference = −1.87 [95% CI: −3.71; −0.03]) (Fig. 2) and with regard to WC there was a decrease of more than 2 cm in the participants who used cannabis and subproducts (mean difference = −2.19 [95% CI: −4.44; 0.06]) (Fig. 3). BMI, on the other hand, showed a slight decrease (mean difference = −0.05 [95% CI: −1.04; −0.94]) (Fig. 4), but body fat was against most of the other groups' results, showing an increase of 0.58% (mean difference = 0.58 [95% CI: −1.75; 2.92]) (Fig. 5).

When evaluating the therapeutic use of cannabis in relation to weight and its subgroups, we obtained a greater decrease in weight in the subgroup that used CB2 receptor antagonist/agonist (mean difference = −2.60 [95% CI: −4.66; −0.54]), and studies with a follow-up time of more than 1 year and studies with fewer than 100 individuals, with mean difference = −2.17 [95% CI: −4.34; −0.00] and −1.98 [95% CI: −5.60; −1.63], respectively. The heterogeneity of the weight assessment and its subgroups can be characterized as high, as demonstrated by the analyses with the highest and lowest values of $I^2 = 99.6\%$ and $I^2 = 96.5\%$ ($p < 0.01$).

In the evaluation of BMI and its subgroups, we obtained a greater reduction in BMI in the subgroup that used Cannabinoid CB1 receptor antagonist/agonist (mean difference = −0.78 [95% CI: −1.80; −0.24]), and in the studies with a follow-up time of more than 1 year and studies with more than 100 individuals, with mean difference = −1.10 [95% CI: −2.23; 0.03] and −0.60 [95% CI: −1.58; 0.38], respectively. The heterogeneity of the BMI assessment and its subgroups of type of cannabis and subproducts and number of individuals can be characterized as high, as demonstrated by the analyses as the highest and lowest values of $I^2 = 99.8\%$ and $I^2 = 99.7\%$ ($p < 0.01$). When analyzing the follow-up time subgroup, we have a moderate heterogeneity of $I^2 = 55.8\%$ for studies of up to one year of follow-up, and high for more than one year, with $I^2 = 99.8\%$ ($p < 0.01$ respectively).

In the evaluation of WC and its subgroups, it was possible to observe an even greater decrease in WC measurements in the subgroup that used Cannabinoid CB1 receptor antagonist/agonist,

**Table 1.** Characteristics and data synthesis of the studies included in the meta-analysis ($N = 12$).

| Authors (Year) | Country(ies) | Study design | Population (*N*, type of subjects, subgroups) | Age (years) | Description of Nutritional Intervention | Relevant observations | Primary outcomes |
|---|---|---|---|---|---|---|---|
| Bergholm et al. [29] | Finland | Double-blind, randomized, placebo-controlled. | $N = 37$<br>IG: 19 (51,35%)<br>CG: 18 (48,64%) | Aged between 35–70 years with MS<br>IG: 57 (48–62)<br>CG: 60 (47–62) | IG: Rimonabant (20 mg)<br>CG: Placebo | Duration: 336 days.<br>Observations: No other anti-obesity agents were used. All treatments were associated with dietary and lifestyle counseling at baseline, after the 1st month, and subsequently every 2nd month until the final study visit. | There was a strong positive correlation between changes in body weight and liver fat content during 48 weeks of weight loss treatment. |
| O'Leary et al. [28] | North America (United States, Canada) and Europe (France, Netherlands, Spain, United Kingdom). | Prospective, multicenter, placebo-controlled, double-blind, randomized, two-arm parallel-group. | $N = 660$<br>IG: 325 (49,24%)<br>CG: 335 (50,75%) | ≥55 years old with abdominal obesity and 2 criteria for MS.<br>Mean age: 62.8 years. | IG: Rimonabant 20 mg<br>CG: Placebo | Duration: Medication once daily for 1338 days.<br>Observations: The entire treatment was associated with usual care in patients with abdominal obesity and MS. | Despite weight loss accompanied by a beneficial change in the cardiometabolic risk factor profile, there was no difference in the progression of mean carotid intima-media thickness (CIMT) between rimonabant and placebo in patients with abdominal obesity and MS, even after 30 months of treatment. |
| Hollander et al. [30] | South Africa; Argentina; United States | Multicenter double-blind, placebo-controlled. | $N = 366$<br>IG: 187 (51,09%)<br>CG: 179 (48,90%) | ≥18 years old with T2DM and insulin monotherapy for ≥ 3 months.<br>IG: 57,4 ± 9,8<br>CG: 58,2 ± 10,9 | IG: Rimonabant 20 mg<br>CG: Placebo | Duration: Medication once a day, before breakfast, for 336 days.<br>Observations: All treatments received instructions to follow a controlled diet and increase physical activity. | The study significantly reduced HbA1c levels and improved multiple cardiometabolic risk factors in T2DM patients receiving various types of insulin monotherapy. |
| Lopez et al. [27] | United States | Randomized, placebo-controlled, double-blind. | $N = 65$<br>IG: 33 (50,76%)<br>M: 16 (48,48%)<br>F: 17 (51,51%)<br>CG: 32 (49,23%)<br>M: 16 (50%)<br>F: 16 (50%) | Between 18 and 55 years old with BMI between 25 to 34.99 kg/m$^2$<br>IG: 57,4 ± 9,8<br>CG: 58,2 ± 10,9 | IG: Hemp oil extract - 60mg (15mg CBD derived from hemp)<br>CG: Placebo (Olive oil) | Duration: Medication once a day, at breakfast, for 42 days.<br>Observations: Throughout the treatment, patients were instructed to maintain their normal eating habits and to adapt their daily physical activities by walking for at least 30 minutes five days a week. | Improvements in HDL cholesterol in overweight healthy men and women. |

**Table 1.** continued

| Authors (Year) | Country(ies) | Study design | Population (*N*, type of subjects, subgroups) | Age (years) | Description of Nutritional Intervention | Relevant observations | Primary outcomes |
|---|---|---|---|---|---|---|---|
| Van Gaal et al. [31] | Europe and United States | Randomized, double-blind pilot study | *N* = 1507<br>IG: 1202 (79,76%)<br>5 mg: 603 (50,17%)<br>10 mg: 599 (49,83%)<br>CG: 305 (20,23%) | ≥18 years old with BMI = 30 kg/m$^2$ or ≥ 27 kg/m$^2$ with treated or untreated HTN or dyslipidemia<br>IG:<br>5 mg: 45.4 ± 11.2<br>20 mg: 44.6 ± 11.9<br>CG: 45.0 ± 11.6 | IG: Rimonabant 5 mg and 20 mg were subdivided into a group receiving 5 mg and a group receiving 20 mg<br>CG: Placebo | Duration: Medication for 365 days.<br>Observations: The entire treatment received dietary counseling and were encouraged to increase physical activity. | Treatment with rimonabant was associated with clinically significant weight loss and additional improvements in waist circumference, lipid concentrations, and insulin resistance, as well as having a favorable safety profile. |
| Alizadeh et al. [36] | Iran | Double-blind, placebo-controlled clinical trial. | *N* = 52<br>IG: 26 (50%)<br>CG: 26 (50%) | Between 18 and 60 years old with BMI of 30–39.99 kg/m$^2$<br>IG: 42.3 ± 8.1<br>CG: 40.6 ± 10.1 | IG: Beta-caryophyllene capsule (containing 100 mg of beta-caryophyllene)<br>CG: Placebo softgel (soybean oil) | Duration: Medication at lunch or dinner, for 56 days. | Effects on improvement of food dependence score in women with obesity diagnosed with this disorder. |
| Jadoon et al. [37] | United Kingdom | Randomized, double-blind, placebo-controlled, parallel-group. | *N* = 62<br>IG: 48 (77,41%)<br>CBD: 13 (27,08%)<br>THCV: 12 (25,0%)<br>1:1 CBD/THCV: 11 (22,91%)<br>20:1 CBD/THCV: 14 (29,16%)<br>CG: 14 (22,58%) | ≥18 years old with T2DM and HbA1c ≤ 10%<br>Mean - 59.0 ± 9.4 years old | IG: CBD; THCV; 1:1 CBD/THCV;20:1 CBD/THCV<br>CG: Placebo | Duration: Medication on an empty stomach, twice a day, 30 minutes before breakfast and 30 minutes before dinner, usually with a 12-hour interval for 91 days.<br>Patients were requested not to modify their eating patterns during the study. Low-dose THCV use. | THCV improved glycemic control and CBD failed to show any detectable metabolic effects despite producing desirable changes in some adipokines and concentrations of intestinal hormones. The incidence of adverse events was similar between treatment groups, and both CBD and THCV were well tolerated. |
| Scheen et al. [32] | 11 countries in Europe, North America, and South America | Randomized, double-blind, placebo-controlled. | *N* = 1045<br>IG: 697 (66,70%)<br>5 mg: 358 (51,36%)<br>20 mg: 339 (48,63%)<br>CG: 348 (33,30%) | Between 18–70 years old with T2DM treated with metformin or monotherapy with sulfonylurea for at least 6 months. In addition to BMI between 27–40 kg/m$^2$, HbA1c (%) from 6.5% to 10%, and fasting glucose 5.55–15.04 mmol/l.<br>IG:<br>5 mg: 45.4 ± 11.2 | IG: Rimonabant 5 mg and 20 mg were subdivided into a group receiving 5 mg and a group receiving 20 mg<br>CG: Placebo | Duration: Medication for 365 days.<br>Observations: Throughout the treatment, patients were advised to follow a slightly hypocaloric diet and to increase physical activity. | Therapeutic efficacy of using rimonabant 20 mg/day in patients with T2DM through effective weight loss, reduction of abdominal adiposity, a clinically significant reduction in HbA1c levels, and improvements in HDL cholesterol, triglyceride concentrations, and systolic blood pressure. |

**Table 1.** continued

| Authors (Year) | Country(ies) | Study design | Population (*N*, type of subjects, subgroups) | Age (years) | Description of Nutritional Intervention | Relevant observations | Primary outcomes |
|---|---|---|---|---|---|---|---|
| | | | | 20 mg: 44.6 ± 11.9<br>CG: 45.0 ± 11.6 | | | |
| Pataky et al. [33] | 7 countries including Finland, France, Netherlands, Portugal, Sweden, Switzerland, and the United States. | Multicenter, randomized, double-blind, placebo-controlled, parallel-group. | *N* = 289<br>IG: 143 (49,48%)<br>CG: 146 (50,52%) | ≥18 and ≤70 years old with BMI ≥30 and ≤45 kg/m$^2$ with a diagnosis of an eating disorder.<br>Mean age: 43.2 ± 10.5 years. | IG: Rimonabant 20 mg<br>CG: Placebo | Duration: Medication once a day, before breakfast, for 182 days.<br>Observations: Throughout the treatment, a slightly hypocaloric diet was recommended. | Significant negative clinical effect on weight loss in obese participants with binge eating disorder. |
| Backhouse et al. [34] | United Kingdom | Randomized, placebo-controlled. | *N* = 21<br>IG: 14 (66,66%)<br>CG: 7 (33,33%) | Women with BMI between 30 and 35 kg/m$^2$ in postmenopause.<br>Mean - 57.8 ± 4.7 years. | IG: Rimonabant 20 mg<br>CG: Placebo | Duration: Medication once a day for 84 days.<br>Observations: Dietary intervention was associated throughout the treatment. | The study showed that the CB1 receptor antagonist rimonabant had metabolic effects independent of weight loss. |
| Van Gaal et al. [35] | Europe and United States | Multicenter, randomized, double-blind, placebo-controlled, parallel-group. | *N* = 886<br>IG: 718 (81,03%)<br>5 mg: 363 (50,55%)<br>20 mg: 355 (49,44%)<br>CG: 168 (19,62%) | ≥18 years old with BMI = 30 kg/m$^2$ or ≥ 27 kg/m$^2$ with treated or untreated HTN or dyslipidemia, with a weight variation of 0.5 kg in the last 3 months.<br>Mean - 45 ± 11.5 | IG: Rimonabant 5 mg and 20 mg were subdivided into a group receiving 5 mg and a group receiving 20 mg<br>CG: Placebo | Duration: Medication for 730 days.<br>Observations: Throughout the treatment, dietary counseling was provided and patients were encouraged to increase their physical activity. | Rimonabant 20 mg produced clinically significant effects on weight loss and improvement in serum lipid, glucose, and insulin levels, which persisted for 2 years with favorable safety and tolerability conditions in patients without a history of severe depressive or anxiety disorders. |
| Carley et al. [38] | United States | Phase II study, multi-site, fully blinded, parallel-group, randomized placebo-controlled clinical trial. | *N* = 56<br>IG: 39 (69,64%)<br>2,5 mg: 19 (48,71%)<br>10 mg: 20 (51,28%)<br>CG: 17 (30,35%) | Between 21 and 65 years old with AHI (Apnea-Hypopnea Index) ≥ 15 and ≤50<br>Mean - 53.6 ± 9.0 | IG: Dronabinol 2,5 mg and 10 mg, were subdivided into GI receiving 2.5 mg and GI receiving 10 mg<br>CG: Placebo | Duration: Medication for 42 days for the CG and IG receiving 2.5 mg; and the IG receiving 10 mg took the medication for 28 days, in order to comply with the drug regulation.<br>Observations: Throughout the treatment, they were instructed to maintain a regular and standard schedule of sleep/wake/activity during their participation. | The study confirms that dronabinol is safe and well-tolerated in individuals with moderate or severe OSA, at the evaluated dosage. |

*M* male, *F* female, *IG* intervention group; *CG* control group, *MS* Metabolic Syndrome, *T2DM* Type 2 Diabetes Mellitus, *HTN* hypertension, *HbA1c* glycated hemoglobin, *BMI* Body Mass Index, *OSA* Obstructive Sleep Apnea.

**Table 2.** Main results should be presented according to the treatment global effect, mean and standard deviation.

| Variables evaluated | Weight total | BMI total | Body fat total | WC total |
|---|---|---|---|---|
| Studies combined | 10 | 8 | 3 | 9 |
| Use of cannabis and subproducts | 2666 | 1417 | 1417 | 2288 |
| Without the use of cannabis and subproducts | 1877 | 930 | 930 | 1511 |
| Mean (95% CI) | −1.87 [−3.71; −0.03] | −0.05 [−1.04; −0.94] | 0.58 [−1.75; 2.92] | −2.19 [−4.44; 0.06] |

*BMI* Body Mass Index, *WC* waist circumference.

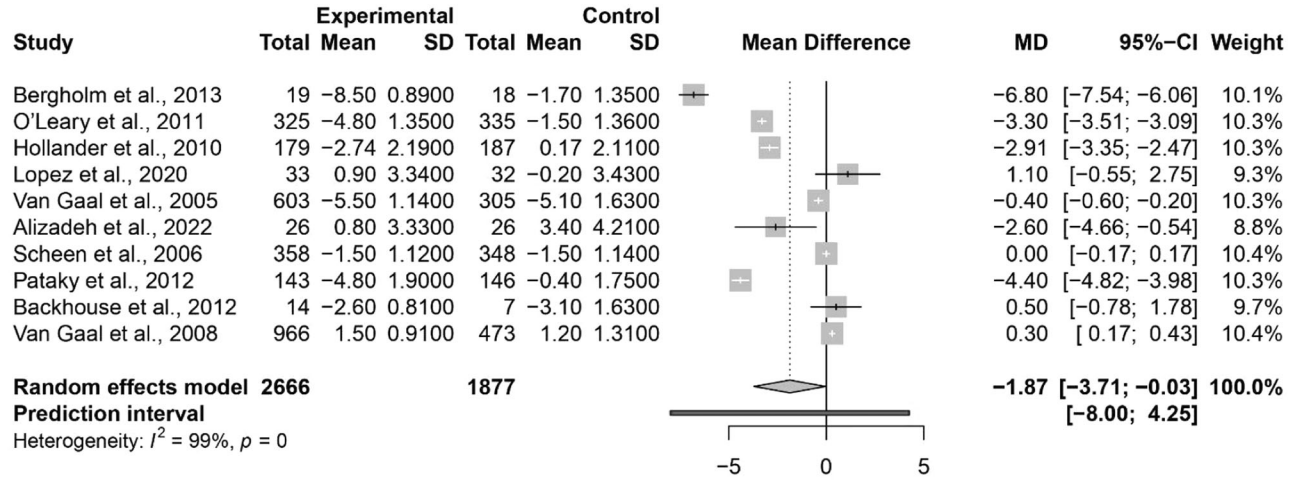


**Fig. 2 Forest plot of the differences in standard means and 95% confidence interval (CI) of the effect of cannabinoid therapeutic use on weight.** MD mean difference, SD standard deviation, CI confidence interval.

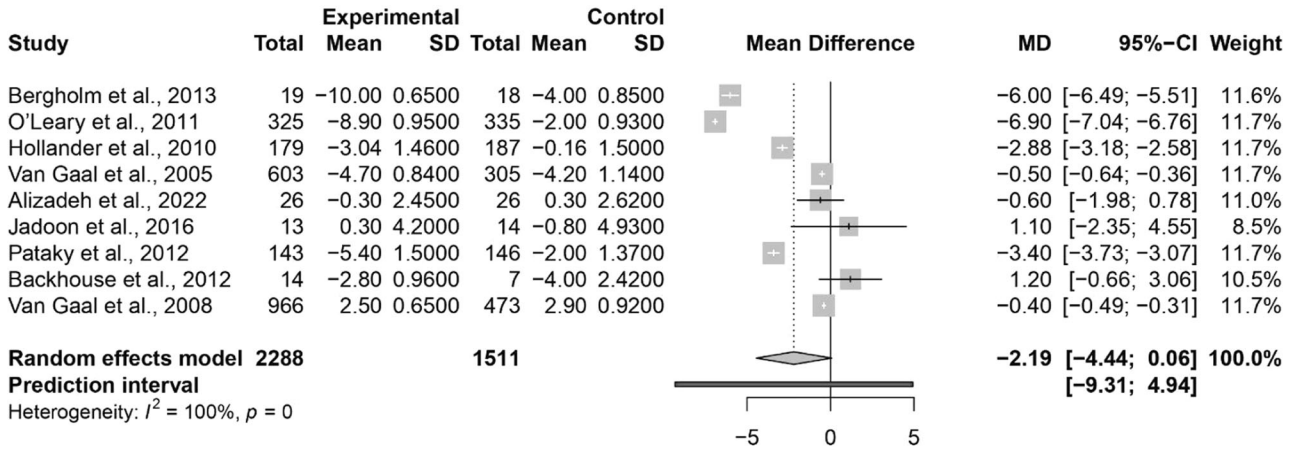


**Fig. 3 Forest plot of the differences in standard means and 95% confidence interval (CI) of the effect of cannabinoid therapeutic use on waist circumference (WC).** MD mean difference, SD standard deviation, CI confidence interval.

with almost 3 cm of loss (mean difference = −2.75 [95% CI: −4. 95; −0.54]), and in studies with a follow-up time of more than 1 year with mean difference = -3.33 [95% CI: −5.59; −0.68] and mean difference = −2.82 [95% CI: −5.15; −0.48], in studies with more than 100 individuals. The heterogeneity of the WC assessment and its subgroups can be characterized as high, as shown by the analyses with the highest and lowest values of $I^2$ = 99.9% and $I^2$ = 92.2% ($p < 0.01$), the latter being represented by the follow-up time of up to one year.

In the evaluation of body fat and its subgroups, due to the low number of studies used, we were unable to obtain a favorable value that was consistent with the rest of the analyses in which only the use of cannabis oil showed a low decrease (mean difference = −0.10 [95% CI: −1.21; 1.01]), and the other types of cannabis and subproducts used showed an increase in body fat, with the Cannabinoid CB1 receptor antagonist/agonist being the highest value found (mean difference = 1.70 [95% CI: 0.66; 2.74]). Even so, the analyses of follow-up time and number of individuals had only 1 subgroup of up to 1 year and less than 100 individuals, mean difference = −0.58 [95% CI: −0.46; 1.63] for both subgroups. With regard to the heterogeneity of the assessment of changes in body composition and its subgroups, all the

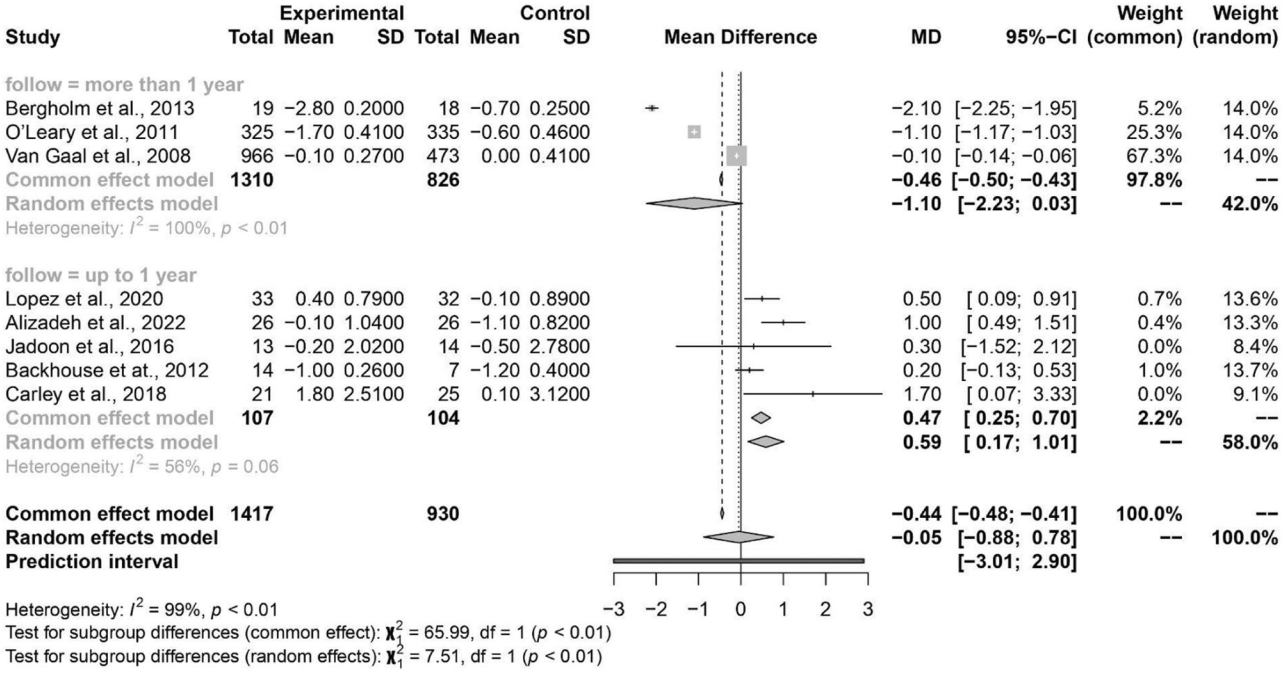


**Fig. 4 Forest plot of the differences in standard means and 95% confidence interval (CI) of the effect of cannabinoid therapeutic use on BMI by follow-up time.** MD mean difference, SD standard deviation, CI confidence interval.

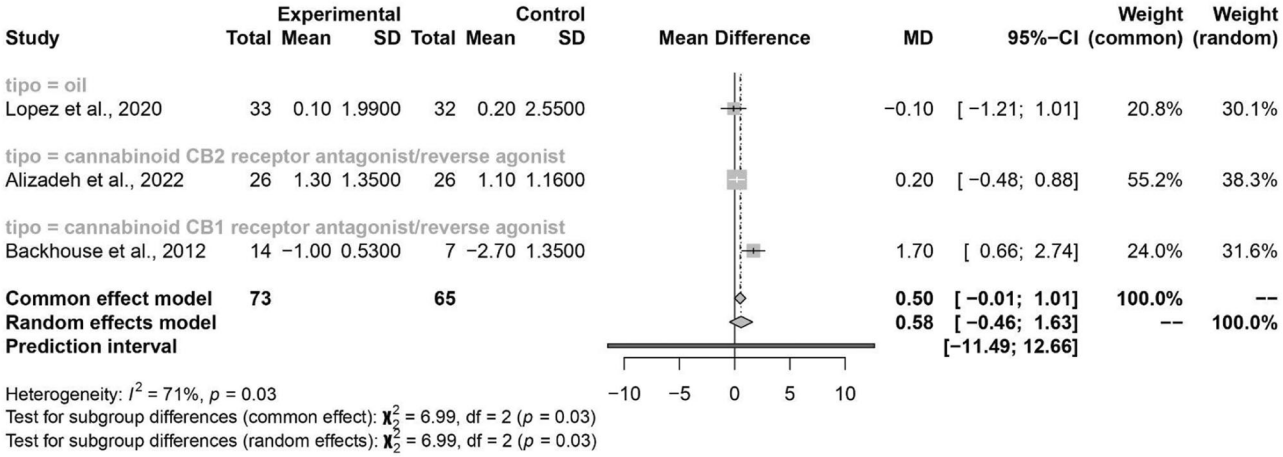


**Fig. 5 Forest plot of the differences in standard means and 95% confidence interval (CI) of the effect of cannabinoid therapeutic use on body fat by type of cannabinoids.** MD mean difference, SD standard deviation, CI confidence interval.

analyses were moderate, as shown by the analyses with $I^2$ values = 71.4% ($p$ < 0.01), which is effectively demonstrated by the low number of studies included in these analyses ($N$ = 3).

## DISCUSSION

From the general comparative analysis of each group, it was possible to see that cannabis and subproducts use resulted in weight reduction and WC. There was a reduction of almost 2 kg in weight of more than 2 cm at WC in the participants who used cannabis and subproducts. When analyzed from the subgroups, BMI showed a greater decrease in relation to the longer follow-up time and body fat, due to the low number of studies included in the analysis ($N$ = 3), was not consistent with the other analyses, with an increase in this percentage by type of cannabis and subproducts, in the case of Cannabinoid CB1 receptor antagonist/agonist (mean difference = 1.70 [95% CI: 0.66; 2.74]). This results reflects the significant importance of adjuvant treatments for reducing anthropometric measurements, and more research is needed to evaluate the use of cannabis and subproducts for this purpose, based on the numerous changes observed in the indices evaluated here.

More than 3000 years ago, the use of *cannabis* as a medicine was first recorded. It has since been used to treat a variety of gastrointestinal and neurological conditions as well as pain, weight loss, and the side effects of chemotherapeutic cancer treatments [5]. It is important to emphasize that changes in physical composition and anthropometric measurements as a result of obesity involve changes to lifestyle and nutritional habits as the first line of treatment [39].

The overburden on public health caused by obesity is now being mentioned by the World Health Organization [2], emphasizing the size of the impact and lack of concern that this has on countries regardless of their level of development.

Because of the changes brought on by the escalation of inflammatory processes and mechanisms, this disease's risk of death is increasing. Thus, the search for strategies to deal with this array of diseases that are fueled by complications brought on by obesity has become the major challenge facing public health on a global scale [4].

The study by Miralpeix et al. [40] states that the deregulation caused by obesity has a fundamental relationship with the hypothalamus, considering it as the "master regulator of energy homeostasis." Since functions related to an organism's food intake and behavior require hypothalamic control through diet-related hormones such as leptin, insulin, and ghrelin. Each cannabis and subproducts receptor interferes with food regulation, either through modulation, such as peristalsis or gastric emptying, or through the stimulation of actions related to appetite and compensatory mechanisms [41]. In order for this to be reflected in the results of reduced anthropometric measurements, the used cannabis and subproducts antagonists have a significant impact, as they promote inhibitory actions on the overall hypothalamic function of the organism in relation to feeding-related hormones, favoring a contrary effect to the physiological mechanism resulting from medication and body composition, which were identified regardless of food intake [42].

The clinical use of CB1 receptor antagonists and reversible antagonists, demonstrated by the loss of weight, BMI, and waist circumference (WC) in our study, can be proven by researchers who have validated this as an anti-obesity medicinal compound. Its ability to decrease appetite also generates metabolic changes in the liver and adipose tissue. What may explain a smaller decrease in BMI compared to weight and WC is that the larger-scale effects on this metric occur after discontinuation of the medication, with chronic use, the same remains in the body for many weeks [39].

Nuesch et al. [43] cites that smaller studies tend to show greater treatment benefits than larger studies, this corroborates the large reduction in weight shown by the CB2 receptor antagonist/agonist subgroup (−2.60 kg [95%CI: −4.66; −0.54]) with a population of less than 100 individuals (−1.98 kg [95% CI: −5.60; −1.63]. As mentioned above regarding the CB1 receptor, the anti-obesogenic factor can also be applied to CB2, which, according to the same study, has a more comprehensive impact on reducing oxidative stress and inflammation [39].

The analysis of body fat contradicts the previously evaluated data, which indicated an increase in body fat in the intervention group. However, this discrepancy can be balanced against the limitations related to the number of studies used, as well as the duration of follow-up and the smaller population that was analyzed. The shorter follow-up period does not favor consistent assessment of the effects of cannabis and subproducts use, as its impact has been debated to persist long after discontinuation, thereby exerting a more significant influence on the results concerning body composition in the long term [44]. A larger number of participants would also enable a more reliable methodological analysis and a broader exploration of the medication's effects [45]. It is therefore hoped that, in order to ensure greater suitability and regulation of this use, the scientific community will provide more scientific bases to guarantee reliability in its use.

## LIMITATIONS AND PROSPECTIVE

The main strengths of this systematic review were that it began with a thorough search of the literature, qualifying it as a low-risk study methodologic, leading to a potential study that could better understand and elucidate the concepts surrounding this topic. Furthermore, our analyses were able to make a comparison with the patient himself, bringing the results closer to reality and ensuring greater statistical efficiency.

Some limitations of our study may be mentioned. First, due to the small number of studies that were conducted, as noted in other studies, this study included only 12 articles in the meta-analysis. Second point is that it is crucial to exercise caution when using cannabis in clinical studies, because its misuse has the potential to be harmful [46].

In addition, some studies did not describe how the patients' food intake was measured, and it was possible not allow for taking into account the previous nutritional status of the evaluated individuals, which could have led to changes in the patient's eating patterns or promoted weight loss/gain prior to the collection of study data, impairing the interpretation of the results.

It is important to analyze that a number of nations continue to focus on legalizing the use of the topic rather than developing studies that could demonstrate its efficacy for use as a therapeutic drug for a variety of diseases, and that this has consequences in various areas, especially from the behavioral and political perspectives of society [47].

Although, there are still obstacles that must be overcome in order to conduct cannabis research, including those related to access, funding, as well as public policies [48] which provide assistance and support for therapeutic use in research and even in diseases where its efficacy has been established. As a result, higher caliber clinical studies are required to confirm the therapeutic use of cannabis and subproducts in changes to body composition, particularly in obesity.

It has been suggested that the medical use of cannabis and its derivatives in the treatment of various illnesses, including obesity, maybe a possibility for the coadjutant treatment of obesity, in particular, due to its promising effects on weight, WC and BMI reduction. However, additional studies that use sound methodological designs and control significant variables, such as intake, diet quality, previous nutritional status and physical activity practice are crucial for the advancement of research in the field. Beyond that, numerous factors may affect the outcome of a meta-analysis; therefore, they must always be carefully considered [49].

## CONCLUSION

This systematic review and meta-analysis revealed that the therapeutic use of cannabis and subproducts reduce weight, WC, and BMI. Furthermore, these analyzes also revealed side effects of increased body fat, which are more noticeable by the relation between exposure time and type of cannabis and subproducts.

However, due to the limited methodologies of included studies caution should be exercised when interpreting the results. The therapeutic cannabis use effects need to be researched in conjunction with isolated physical activity and dietary interventions in order to bring about greater possibilities for the prevention of obesity in public health.

## DATA AVAILABILITY

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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## AUTHOR CONTRIBUTIONS

AJFF and NSG developed the study's concept and projected it. Direct access to DRT, MGR, AJFF, and NSG; data verification and analysis. MGR and NSG wrote the first paragraph of the manuscript. All of the authors contributed to the interpretation of the data, reviewed and edited the manuscript. NSG oversaw the research process. All of the authors had complete access to all of the study's data and were ultimately responsible for the decision to submit them for publication.

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## COMPETING INTERESTS

The authors declare no competing interests.

## ADDITIONAL INFORMATION

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