

Substance abuse and weight control

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Obesity Medicine

Substance abuse and weight control: Do they really have opposing effects?

--Manuscript Draft--

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| Manuscript Number: | |
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| Abstract: | <p>Introduction: On clinical practice, commonly patients are afraid to treat their substance abuse and has as consequence an increase in addiction for food, increasing in their body weight without control. Intuitively, it makes sense, considering addiction for food and drugs may share the same neuronal pathway in the brain, but no study seems to have confirmed this hypothesis. We did a systematic review to integrate the findings of all interventional studies investigating the relation between substance abuse and weight management treatment. Methods: The Pubmed (Medline) search, led us to include 8 studies. Results: None of the three studies testing drug interventions on cigarette cessation increased body mass; and two of them reported a reduction in body weight and BMI of the abstinent subjects being treated. The five studies testing drug interventions, behavioral counseling groups or bariatric surgery aiming weight reduction, did not increase the addiction for cigarette or alcohol; and incipient evidence from these studies pointed to higher number of smoke abstinent individuals among the normal weight than obese ones following intervention and reduced number of cigarettes per day with the intervention. Conclusion: The majority of evidence from interventional studies showed that weight management and drug abuse treatment are complementary to each other and may be a good combination to treat drug addiction in overweight and obese individuals.</p> |
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| Opposed Reviewers: | |

February, 26, 2021

Dear Editor

We submitted the manuscript entitled “**Substance abuse and weight control: Do they really have opposing effects?**” for your consideration as a short communication. All co-authors have reviewed and approved the contents of the manuscript and there is no financial interest to report. Manuscript has been submitted solely to Obesity Medicine and that it has not been previously published, either completely or in part, nor have the findings been posted online. Therefore, as the main author I state that have had access to all aspects of research including writing process and take all responsibility for the manuscript.

We submitted as short communication given that our review was very objective and showed important opposing results comparing to what is expected. On clinical practice, commonly patients are afraid to treat their substance abuse (mainly cigarette addiction) and has as consequence an increase in addiction for food, increasing in their body weight without control. However, the majority of evidence from interventional studies showed that weight management and drug abuse treatment are complementary to each other and may be a good combination to treat drug addiction in overweight and obese individuals.

Since the journal is interested in interdisciplinary prevention and treatment of obesity, we believe the theme fits to the journal scope and may be very important specially now, during COVID-19 pandemic, where people have reported higher uncontrolled addiction and feeding behavior. We thank in advance for the attention with the manuscript and we are looking forward to see your response regarding our submission.

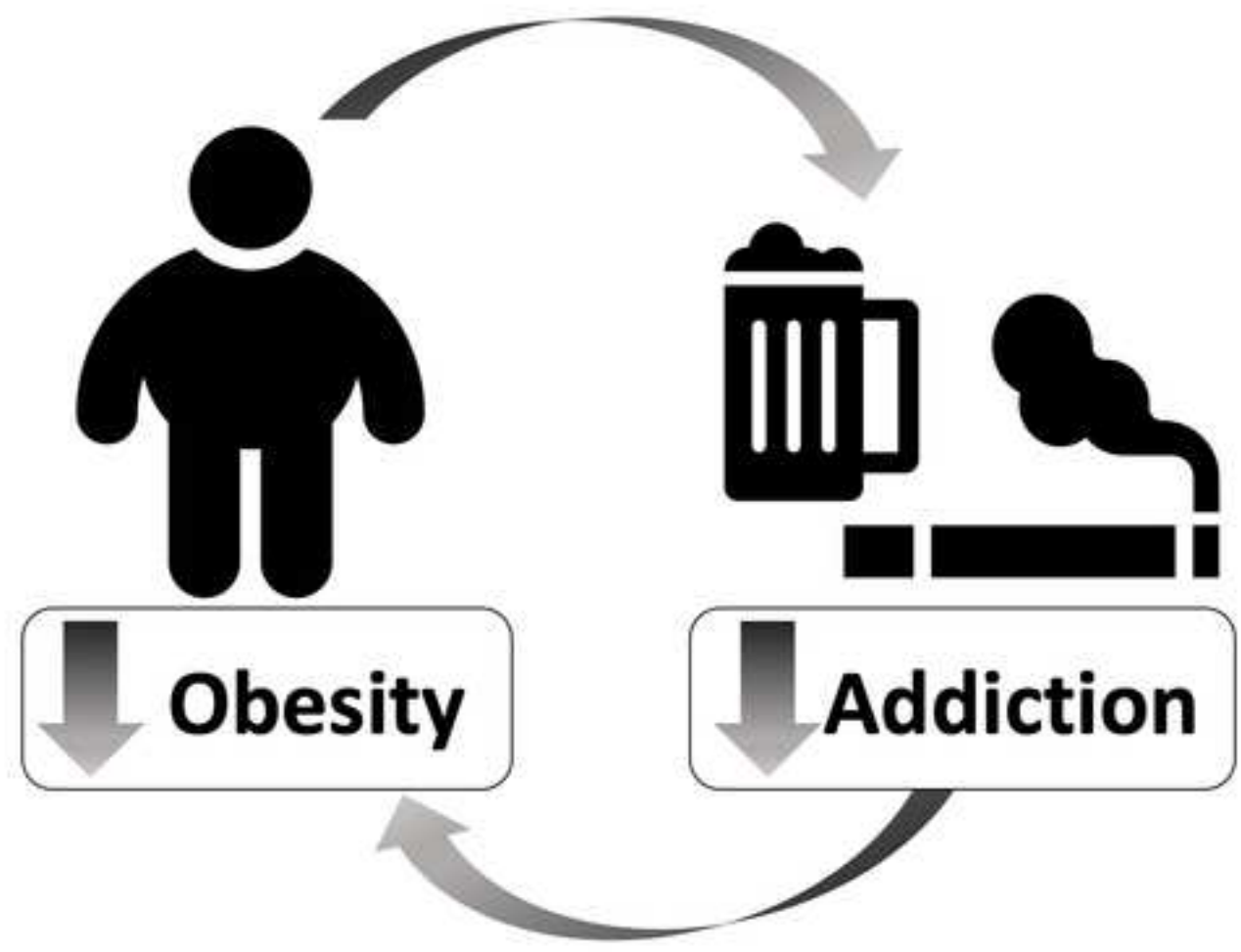
Kind regards,

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Highlights

- Drug interventions for cigarette cessation did not increase body mass.
- There was reduction in body weight and BMI in abstinent subjects under drug treatment.
- None of the diverse interventions aiming weight reduction, increase the addiction for cigarette or alcohol.



Substance abuse and weight control: Do they really have opposing effects?

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Abstract

Introduction: On clinical practice, commonly patients are afraid to treat their substance abuse and has as consequence an increase in addiction for food, increasing in their body weight without control. Intuitively, it makes sense, considering addiction for food and drugs may share the same neuronal pathway in the brain, but no study seems to have confirmed this hypothesis. We did a systematic review to integrate the findings of all interventional studies investigating the relation between substance abuse and weight management treatment. **Methods:** The Pubmed (Medline) search, led us to include 8 studies. **Results:** None of the three studies testing drug interventions on cigarette cessation increased body mass; and two of them reported a reduction in body weight and BMI of the abstinent subjects being treated. The five studies testing drug interventions, behavioral counseling groups or bariatric surgery aiming weight reduction, did not increase the addiction for cigarette or alcohol; and incipient evidence from these studies pointed to higher number of smoke abstinent individuals among the normal weight than obese ones following intervention and reduced number of cigarettes per day with the intervention. **Conclusion:** The majority of evidence from interventional studies showed that weight management and drug abuse treatment are complementary to each other and may be a good combination to treat drug addiction in overweight and obese individuals.

Keywords: Substance-Related Disorders, Smoke, Alcoholics, Obesity.

please insert Abstract figure

Introduction

Abuse of substances such as nicotine and alcohol can be very damaging for health (1). Nicotine abuse increases risk factors for example, dyslipidemia reducing HDL, hypertension vessels narrowing increasing the chances of acute coronary and cerebrovascular events such as infarction, stroke and sudden death (2). Alcohol abuse led to high-blood pressure, increasing LDL, cholesterol and possibly arrhythmias as well as cancer mostly common in head and neck. Furthermore, the addition of both substances has been associated with obesity (3).

On clinical practice, commonly patients are afraid to treat their substance abuse and has as consequence an increase in addiction for food, increasing in their body weight without control. Intuitively, it make sense, considering addiction for food and drugs may share the same neuronal pathway in the brain (4). In fact, cross-sectional studies show that following smoking abstinence, smokers gain an average of 5–10 pounds (5,6), reaching a mean of 13 pounds at 1 year (11) and 21 pounds over 5 years (7). In the other hand, the actual weight gain following smoking abstinence has been associated with smoking relapse(8), suggesting that not exactly the smoke abstinence is the cause of weight gain but likely the psychological challenges surrounding this issue.

Curiously, higher chance of substance abuse, such as nasal spray has been noticed in obese individuals compared to normal weight individuals (9) and there is a high chance of being overweight or obese among alcohol- and nicotine-dependent individuals (10). However, interventions to reduce body weight concomitantly reduce the addiction for difference substances. For example, the use of bupropion plus Naltrexone reduced the number of cigarettes (11) and bariatric surgery reduced the number of drinks per month (12).

The Combination of Varenicline and Lorcaserin for Tobacco Dependence Treatment also prevented weight gain in obese smokers (13), suggesting both benefits can be acquired simultaneously. These relations have never been addressed in a systematic review, and there is no consensus about the effects of each treatment for substance abuse and weight management.

Thus, this systematic review aims to identify what is the effect of weight management therapies on substance abuse and the effect of substance abuse interventions on body weight.

Methods

A systematic search was conducted on Pubmed (MEDLINE) with the last update on April 20, 2020, using the following syntax: (((“Drug abuse” [tiab] OR “Substance-Related Disorders”[mh] OR “Smoke”[mh] OR “Cocaine”[mh]OR“Alcoholics”[mh]OR “Marijuana Abuse”[mh]) AND (“obesity”[mh])) AND (“Therapeutics”[mh]OR “therapy” [Subheading]) AND (“Clinical Trial”[Publication Type] OR “Clinical Trials as Topic”[mh]))

The inclusion criteria were: (1) studies testing any weight management or drug abuse intervention; (2) assessing as outcomes body weight, body mass index (BMI), number of drinks when they were alcoholic and number of cigarettes or percentage of abstinent individuals when they were cigarette addicts; (3) studies written in English Language; (4) assessing human participants.

We extract data regarding the effects of weight management treatment on drug abuse and the effects of drug abuse treatment on weight management. The results of

each intervention were reported individually, based on each study statistical analysis, since no quantitative synthesis was not possible for the variety of designs found.

Results and Discussion

Details of the studies' selection process are described in Figure 1. Among the 48 studies, 8 met our inclusion criteria (9–16).

****please insert Figure 1 here****

Although we did not exclude any type of drug abuse, all the studies investigating the changes in body weight and composition after drug abuse treatment, studied overweight or obese individuals quitting smoking (Table 1). The studies investigating the effects of weight management treatment in individuals with addiction, tested the short-term effect of bariatric surgery, or 4 to 24 weeks intervention with medications such as Naltrexone and bupropion, d-Fenfluramine 30 mg, transdermal Nicotine Therapy, Nasal Spray Therapy and behavioral interventions (Table 1). Those individuals were alcoholic or cigarette addicts (Table 1).

****please insert Table 1 here****

Regarding the ones testing the effect of drug abuse treatment on weight management, they treat cigarette addiction with different medications from 4 to 26 weeks. **Hurt et al.** (13), did not observed any significant changes in body mass, body

mass index or waist circumference in overweight and obese smokers who maintained prolonged smoking abstinence following 26 weeks of combined treatment with Varenicline 1 mg/2x/d and Lorcaserin 10mg/2x/d. On the other hand, **Floden et al.** (16), achieved body mass index reduction in overweight and obese adolescent smokers abstinent after 6 weeks using Bupropion 300mg/day. In the same way, **Spring et al.** (15) confirmed a body mass reduction after 4 weeks treatment with D-fenfluramine 30 mg in overweight individuals after smoking cessation. Taken these findings together, is clear that overweight and obese individuals may not fear the weight gain and likely they can expect to reduce they body wait when undergo a specific drug treatment for smoke cessation.

None of the five studies testing the effect of weight management treatment on drug abuse found increase in addiction symptoms. In fact, some of them showed reduction of those symptoms. At 24 weeks of follow-up with different interventions (Behavioral group counseling plus 8 weeks Transdermal Nicotine Therapy or Nasal Spray Therapy), **Lerman et al.** (9) showed higher number of abstinent individuals among the normal weight than obese ones. At last, **Wilcox et al.** (11) aiming to stimulate smoking cessation and mitigate weight gain, found 24 weeks of Naltrexone (32 mg/day) and bupropion (360 mg/day) plus behavioral counseling reduced the number of cigarettes per week but no reduction of body weight. Furthermore, **Love et al. and Spring et al.** (14,15) despite no statistical significance showed higher number of abstinent smoking individuals in weight management interventions than control groups.

It is noteworthy, the effects of Roux-en-Y gastric bypass surgery are completely different of the drugs and behavioral intervention. Pepino et al. (12), found that after surgery alcoholic individuals had both earlier blood alcohol concentration peaks and

greater feeling of drunkenness, which in some way can bring other public safety and clinical implications.

Conclusion

The literature does not support the concern about gain weight when individuals treat drug abuse. In opposition, there is more evidence that weight management and drug abuse treatment are complementary to each other and may be a good combination to treat drug addiction in overweight and obese individuals. Despite some investigations on alcoholic individuals, the significant positive effects were observed in studies investigation cigarette addiction treatment. More studies will be necessary to prove these incipient findings with a robust meta-analysis.

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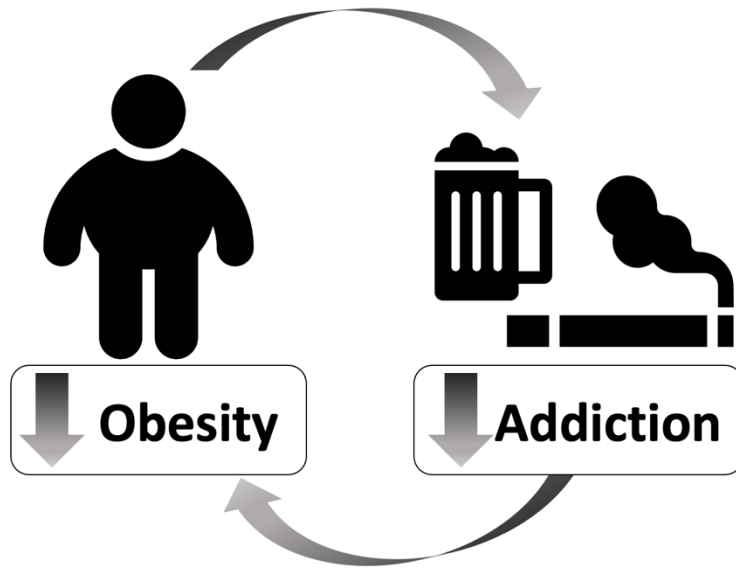
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Figures



Abstract figure. Reduction in body weight favoring reduction of addiction and vice-versa.

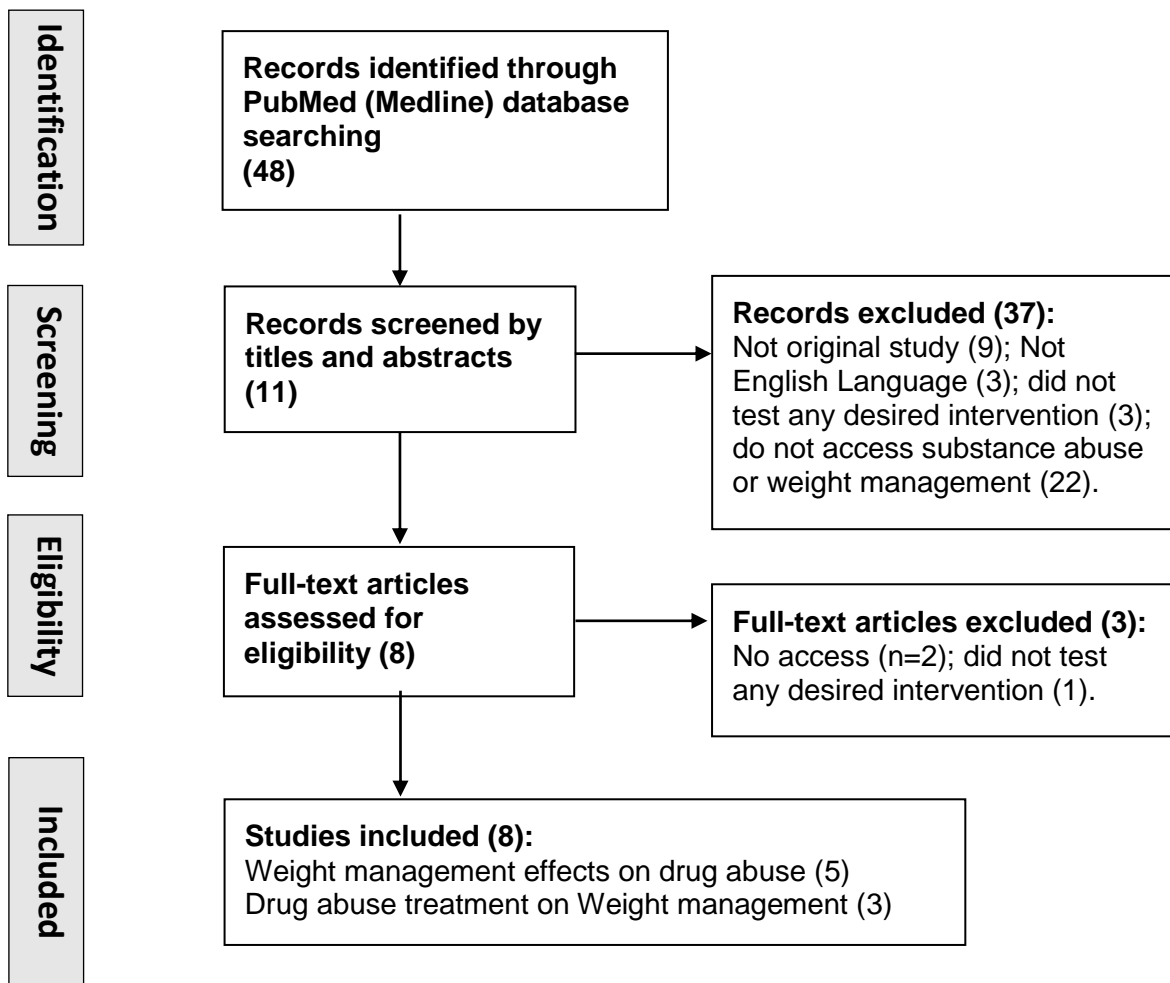


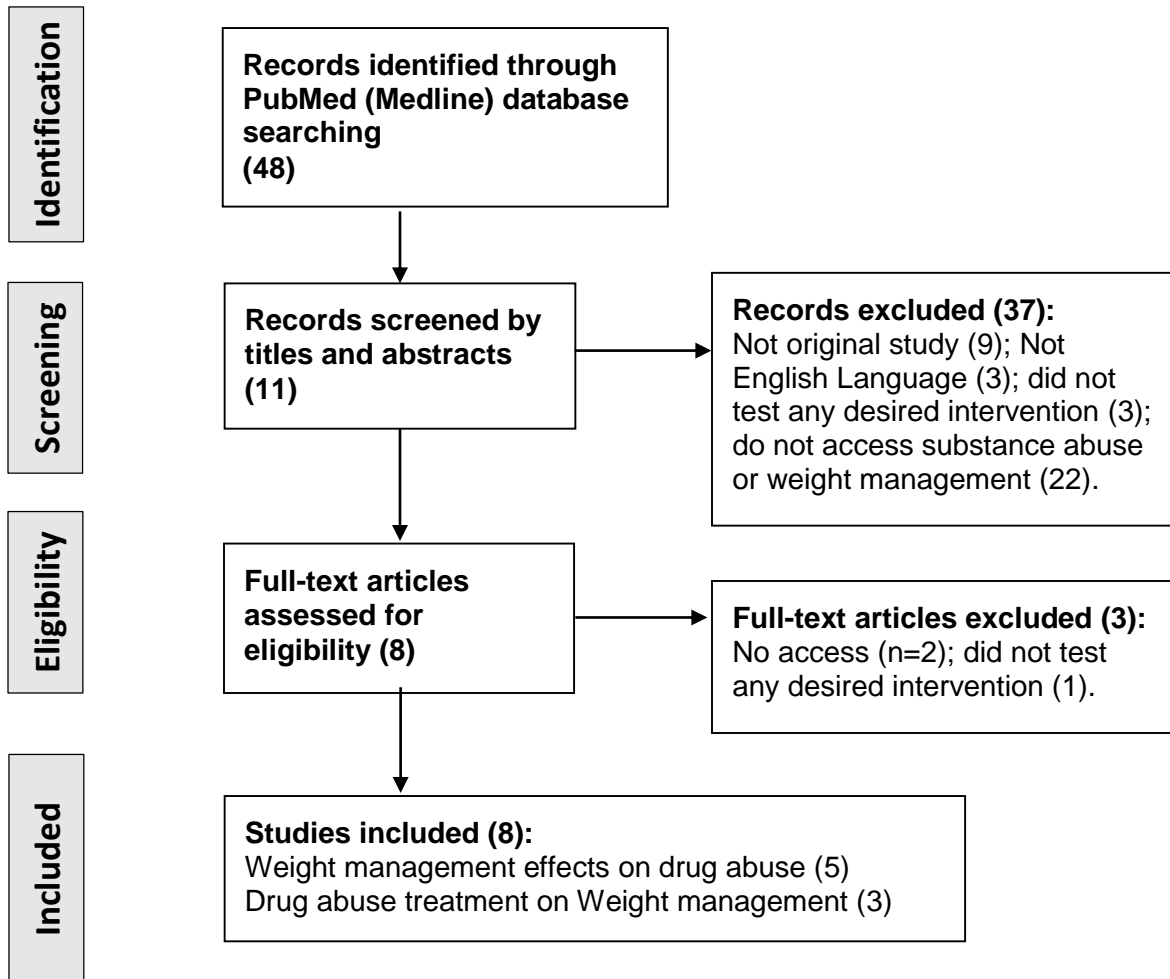
Figure 1. Flowchart of study selection.

Table 1. The effects of weight management treatment on drug abuse and the effects of drug abuse treatment on weight management.

| Studies | Participants | Intervention | Study design | Results/ effects direction | Favored (Statistically) | Number of patients |
|--|---|--|--|--|-------------------------|--------------------|
| Effect of drug abuse treatment on weight management | | | | | | |
| Hurt, 2017 | Overweight or obese smokers who maintained prolonged smoking abstinence | Varenicline 1 mg/2x/d and Lorcaserin 10mg/2x/d | 12 weeks | ↑ body mass within abstinent individuals (1.1: 90% CI: -0.9, +3.1kg) | No difference | 10 |
| | | | | ↑ body mass index within abstinent individuals (0.3: 90% CI: -0.3, +1.0 kg/m ²) | No difference | 10 |
| | | | | ↑ WC within abstinent individuals (0.2: 90% CI: -2.9, +3.4cm) | No difference | 10 |
| | | | 26 weeks | ↑ body mass within abstinent individuals (6.4: 90% CI: -0.3, +13.1kg) | No difference | 6 |
| | | | | ↑ body mass index within abstinent individuals (1.9: 90% CI: -0.1, +3.9kg/m ²) | No difference | 6 |
| | | | ↑ WC within abstinent individuals (2.2: 90% CI: -3.4, +7.9 cm) | No difference | 6 | |
| Floden, 2016 | Overweight and obese adolescent smokers abstinent | Bupropion 150mg/d | 6 weeks | ↓ BMI z score (0.04: -0.17, 0.08, p=0.44) | No difference | 101 |
| | | Bupropion 300mg/d | 6 weeks | ↓ BMI z score (-0.19: -0.29, -0.04, p=0.01) | Intervention | 105 |
| Spring, 1991 | Overweight individuals after smoking cessation | D-fenfluramine 30 mg | 4 weeks | ↓ body mass for intervention group (-1.8 ± 5, p<0.05) and ↑ body mass for control group (3.5 ± 1.3lb, p<0.001) | Intervention | I:16/C:15 |
| Effect of weight management treatment on drug abuse | | | | | | |
| Pepino, 2015 | Alcoholic | Roux-en-Y Gastric Bypass Surgery: | Post-surgery intervention | → N of drinks/d/mo in the past 6mo (1.3 ± 0.4 vs 0.8 ± 0.8) | No difference | 5 |
| | | | | → N of drinks/d in the past 6mo (2.8 ± 1.6 vs. 1.9 ± 2.4) | No difference | 5 |
| | | | | → N of standard drinks given on alcohol challenge test (1.8 ± 0.2 vs. 1.7 ± 0.2) | No difference | 5 |
| Wilcox, 2010 | Smokers | Naltrexone (32 mg/d) | 24 weeks | ↓ n of cigarettes /week (-110±49, p<0.001) | Intervention | 129 |

| | | | | | | |
|--------------|--------------------|--|----------|--|---------------------|-----------|
| Love, 2010 | Smokers | and bupropion (360 mg/d) plus behavioral counseling Weight management intervention | 24 weeks | > percentage of abstinent post intervention than control (33.3% vs. 20.3%) | No difference | I:27/C:74 |
| Spring, 1991 | Overweight smokers | d-Fenfluramine 30 mg | 4 weeks | > percentage of abstinent post intervention than control (55% vs 33.3%) | No difference | I:16/C:15 |
| Lerman, 2004 | Smokers | Behavioral group counseling plus 8 weeks Transdermal Nicotine Therapy or Nasal Spray Therapy | 24 weeks | > higher number of abstinent individuals among the normal weight than obese ones (OR 0.39:CI 95%: 0.15 - 1.01, p=0.05) | Normal weight group | 299 |

Legend: I: intervention; C: control; OR odd ratio; CI confidence interval; WC: waist circumference; Arrows indicate the direction of variation with intervention (↑= increase, ↓= reduction and → = no change); > higher values compared to control group at post intervention; < lower values compared to control group at post intervention; BAC: blood alcohol concentration; d: days; mo: months.



CONFLICT OF INTEREST

The authors declare no conflict of Interest for the manuscript
“Substance abuse and weight control: Do they really have opposing
effects?” submitted to Obesity medicine journal.

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