

# Continuous and intermittent sibutramine were equally effective at 44 weeks for reducing weight in obese persons

Wirth A, Krause J. Long-term weight loss with sibutramine: a randomized controlled trial. *JAMA*. 2001 Sep 19;286:1331-9.

## QUESTION

In obese persons, is sibutramine effective for reducing weight?

## DESIGN

Randomized (allocation concealed\*), blinded (investigators and patients),\* placebo-controlled trial with 44-week follow-up after randomization.

## SETTING

108 private practices and 3 hospital outpatient departments in Germany.

## PATIENTS

1001 patients who were 18 to 65 years of age (mean age 43 y, 77% women), had a body mass index (BMI) of 30 to 40 kg/m<sup>2</sup>, and had ≥ 1 previous unsuccessful attempt at losing weight by using dietary measures. Exclusion criteria were serious cardiovascular or metabolic diseases; history of drug or alcohol abuse; need for antidepressants, β-blockers, or any drugs influencing body weight; or inadequate contraception in women of childbearing age. 79% of patients completed the study; all patients were included in the analysis.

## INTERVENTION

Patients who responded (i.e., weight loss of ≥ 2% or ≥ 2 kg) to sibutramine, 15 mg/d, during a 4-week run-in period were allocated to 1 of 3 groups for 44 more weeks: continuous sibutramine, 15 mg/d (*n* = 405); intermittent sibutramine, 15 mg/d during weeks 1 to 12, 19 to 30, and 37 to 48 (*n* = 395); or placebo (*n* = 201).

## MAIN OUTCOME MEASURE

Weight loss.

## MAIN RESULTS

Analysis was by intention to treat. Mean weight loss at 44 weeks after randomization was 3.8 kg (95% CI 3.2 to 4.4) for continuous sibutramine and 3.3 kg (CI 2.7 to 4.0) for intermittent sibutramine; patients in the

placebo group gained weight (mean 0.2 kg, CI -0.6 to 0.9) (*P* < 0.001 for the difference between each treatment group and placebo). More patients in each of the treatment groups than in the placebo group lost 5% and 10% of their baseline weight (*P* < 0.001 for all comparisons) (Table). The 2 treatment groups did not differ for weight loss.

## CONCLUSION

In obese persons, continuous or intermittent sibutramine were equally effective for reducing weight.

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\*See Glossary.

## Continuous sibutramine (CS), intermittent sibutramine (IS), or placebo for obesity†

Outcomes at 44 wk	Comparisons	Event rates	RBI (95% CI)	NNT (CI)
5% weight loss	CS vs placebo	65% vs 35%	86% (54 to 130)	4 (3 to 5)
	IS vs placebo	63% vs 35%	81% (49 to 123)	4 (3 to 6)
10% weight loss	CS vs placebo	32% vs 13%	148% (71 to 266)	6 (4 to 9)
	IS vs placebo	33% vs 13%	154% (75 to 276)	6 (4 to 8)

†Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

## COMMENTARY

Given the unabating rise in obesity prevalence, our treatment armamentarium clearly leaves something to be desired. Pharmacologic choices are limited and have a questionable safety record, and none is impressively effective. The study by Wirth and Krause of sibutramine, an anorexigenic noradrenaline and serotonin-reuptake blocker available since 1998, is of some interest to clinicians who are challenged by the prospect of helping their obese patients. The interest in this study is not so much because of its redundant finding that sibutramine has a modest salutary effect over placebo for initial weight loss but because it showed that intermittent treatment (about 75% of the time on, 25% of the time off) was about as effective as continuous treatment. One 36-week controlled trial of an older agent, phentermine, also found this effect when alternating 4-week blocks of time on and off the drug (1).

Since most patients I see take antiobesity medications in an intermittent fashion anyway, this finding is reassuring. Intermittent use is often probably safer than the never-ending treatment of obesity that is often advocated but has yet to be shown effective in studies of > 2 years. Whether any antiobesity agent that acts systemically will prove entirely

safe in the long term is, unfortunately, unknown. Sibutramine has certain known problems, notably its propensity to raise blood pressure and pulse (in part undermining one of the main reasons to use it in the first place). Nonetheless, sibutramine has some proven efficacy, and we should not hold antiobesity drugs to a higher standard than drugs used to control hypertension or diabetes. If only we had as many good choices and combinations for obesity as we do for hypertension and diabetes: To begin with, we would not need to treat nearly as many patients for the latter two.

Given the high stakes, we have no choice but to keep trying to find effective and safe pharmacologic and other treatments for obesity. Basic science and pharmacology will no doubt uncover further options as the years unfold.

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## Reference

- Munro JF, MacCuish AC, Wilson EM, Duncan LJ. Comparison of continuous and intermittent anorectic therapy in obesity. *Br Med J*. 1968;1:352-4.