

# TEN PERCENT OR GREATER WEIGHT LOSS IS A CLINICALLY MEANINGFUL OUTCOME IN THE TREATMENT OF OBESITY

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## REVISED ABSTRACT

**Purpose:** Health plans vary widely in their coverage and reimbursement policies for obesity treatments, in part due to a lack of consensus about the degree of weight loss that will confer obesity-related morbidity risk reduction. Although a weight loss of 5-10% has been associated with clinical benefits, NIH obesity guidelines state that the goal of obesity treatment should be a loss of at 10% or greater of baseline weight. This review examines the literature on weight loss and associated clinical outcomes to determine whether a 10% weight loss threshold should be considered clinically meaningful.

**Method:** We compared the long-term effects (minimum study duration 1 year) of at least 10% intentional weight loss versus <10% weight loss among overweight and obese adults on biomarkers of obesity-related health risks, including lipids; blood pressure; and glycemic, insulinemic, and inflammatory markers. Relevant studies were identified through a Medline search (1966-2009) of English studies using the following MeSH terms: "weight loss (major heading)," "cardiovascular diseases/metabolism," "cardiovascular diseases/physiology" "cardiovascular diseases/prevention and control," "lipids/blood," "blood pressure," "blood glucose," "insulin resistance," and "glycosylated hemoglobin A." Studies with a mean weight loss ≥20% were excluded.

**Result:** Among 1,456 citations, 19 were identified as relevant. Weight loss ≥10% is associated with improved blood pressure, glycemic, inflammatory, and lipid outcomes. Compared to <10% weight loss, a weight loss of ≥10% confers a significantly greater reduction in systolic and diastolic blood pressure among overweight/obese persons. A weight loss of 10% or more is associated with a 1.6% and 1.2% decrease in hemoglobin A1c, and a 33% reduction in mortality among overweight and obese persons with type 2 diabetes. Severely obese persons who sustained a mean weight loss of 16% had a 75% decrease in the 10-year incidence of type 2 diabetes. The greatest improvements in biomarkers of obesity-related inflammation have been seen in studies achieving ≥10% weight loss. Sustained weight loss of ≥10% improves hyperlipidemia, especially among persons with high baseline cholesterol levels.

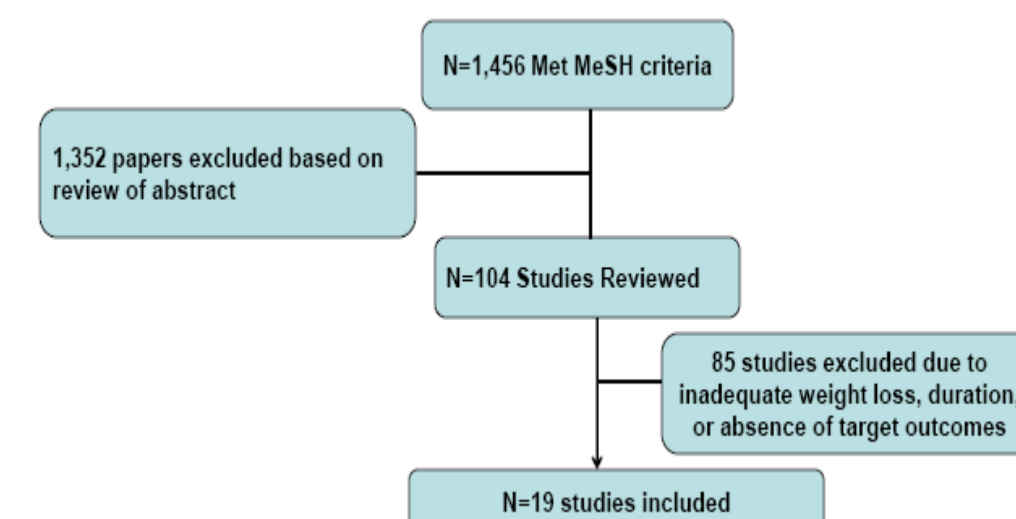
**Conclusion:** Weight loss of ≥10% confers substantial cardiovascular and metabolic benefits among overweight and obese adults, and appears to be a more clinically significant intermediate marker of the effectiveness of weight loss interventions. Consistent application of this benchmark by health plans in determining coverage and reimbursement for weight loss interventions may result in wider access to more effective treatments and reduce the escalating rate of obesity-related diseases and related spiraling medical costs.

## BACKGROUND

- A growing body of literature has demonstrated that a 5-10% weight loss confers significant reductions in cardiometabolic risks associated with obesity-related illnesses.<sup>1,2</sup>
- However, long-term health benefits may be maximized with sustained weight loss of ≥10% of initial body weight. The NIH guidelines recommend that overweight/obese persons initially reduce their body weight by at least 10% and maintain that weight loss for 1 year.<sup>3</sup>
- This review focuses on the health benefits that have been associated with a weight loss of ≥10% sustained for at least 1 year.

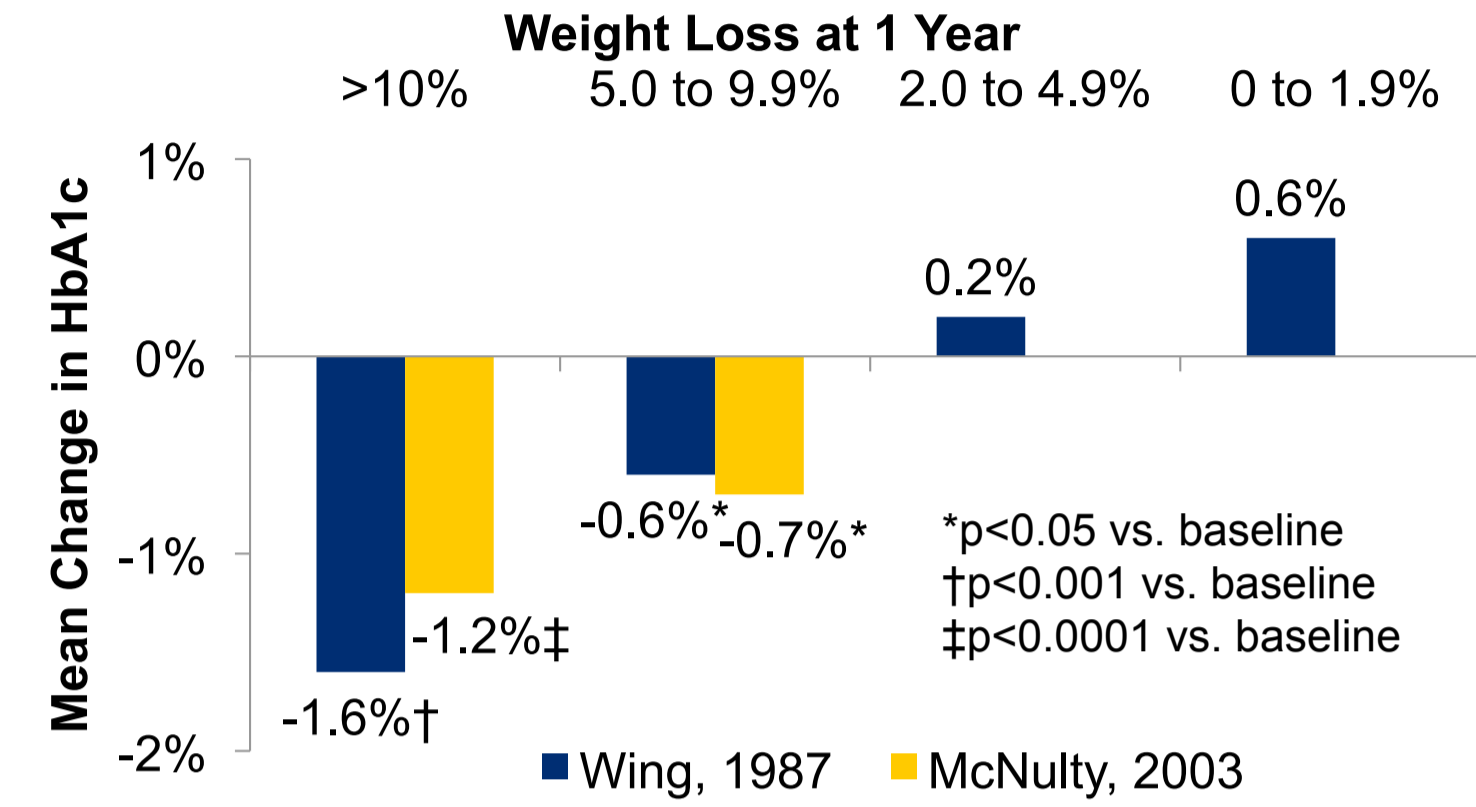
## METHODS: STUDY IDENTIFICATION

- Included studies were prospective clinical trials with duration ≥1 year, adults only (>18 years old), mean percentage weight loss from baseline ≥10% and <20% reported for at least one group; statistical significance reported for within-group change for targeted obesity-related biomarkers.
- Nonhuman studies, case reports, reviews, and editorials were excluded.
- A Medline search was conducted of English-language studies published from 1966 to 2009 using the MeSH terms: "weight loss (major heading)," "cardiovascular diseases/metabolism," "cardiovascular diseases/physiology" "cardiovascular diseases/prevention and control," "lipids/blood," "blood pressure," "blood glucose," "insulin resistance," and "glycosylated hemoglobin A."



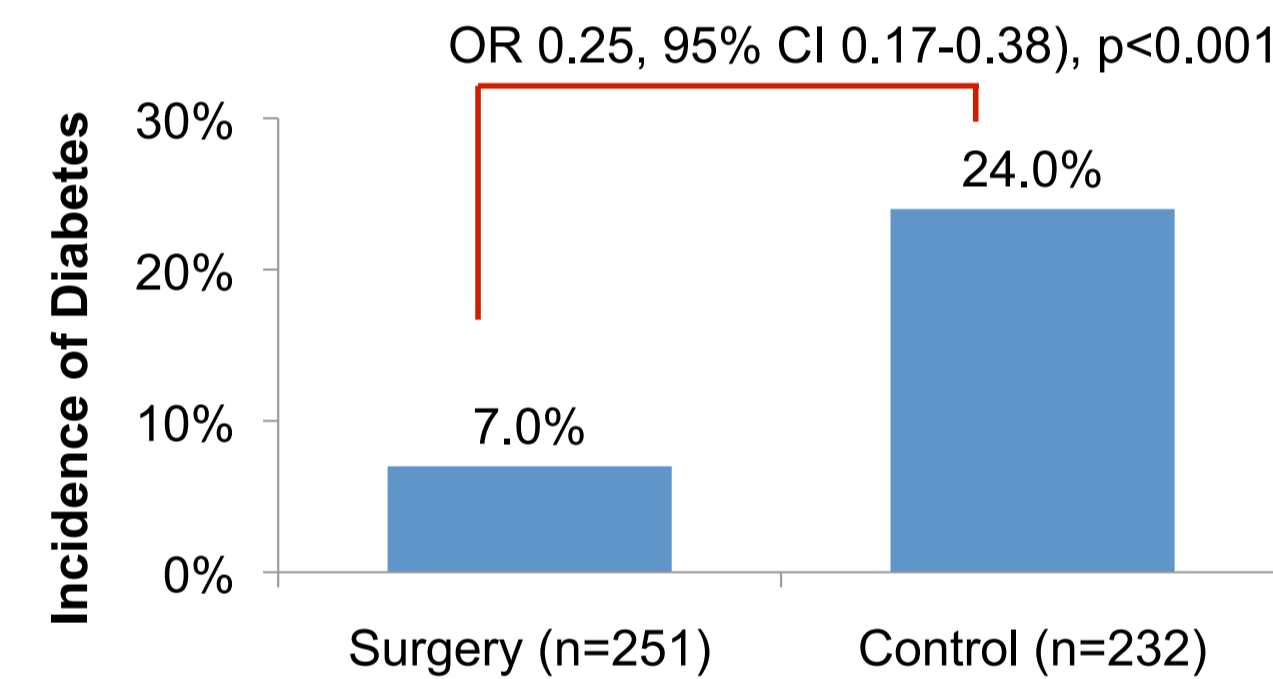
## RESULTS: EFFECT OF ≥10% WEIGHT LOSS ON HbA1c

Change in HbA1c as a Function of % Weight Loss Among Obese Patients with Type 2 Diabetes<sup>4,5</sup>



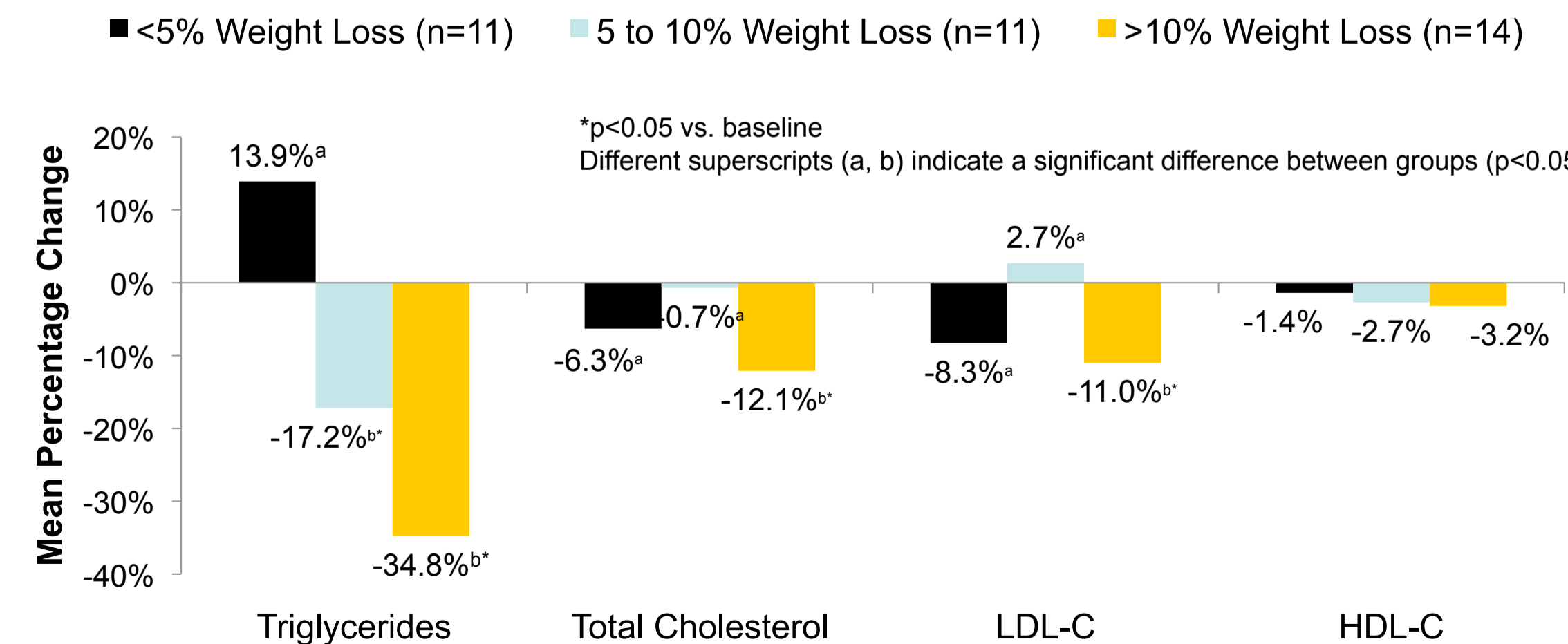
## RESULTS: EFFECT OF ≥10% WEIGHT LOSS ON DIABETES INCIDENCE

Incidence of Diabetes at 10 Years Among Obese Patients Who Underwent Bariatric Surgery (Mean Weight Loss 16.1%) Compared with Matched Controls (0% Weight Loss)<sup>6</sup>



## RESULTS: EFFECT OF ≥10% WEIGHT LOSS ON LIPIDS

Change in Lipids at 2 Years by Magnitude of Weight Loss Among Women with Baseline Total Cholesterol ≥200 mg/dL<sup>7</sup>

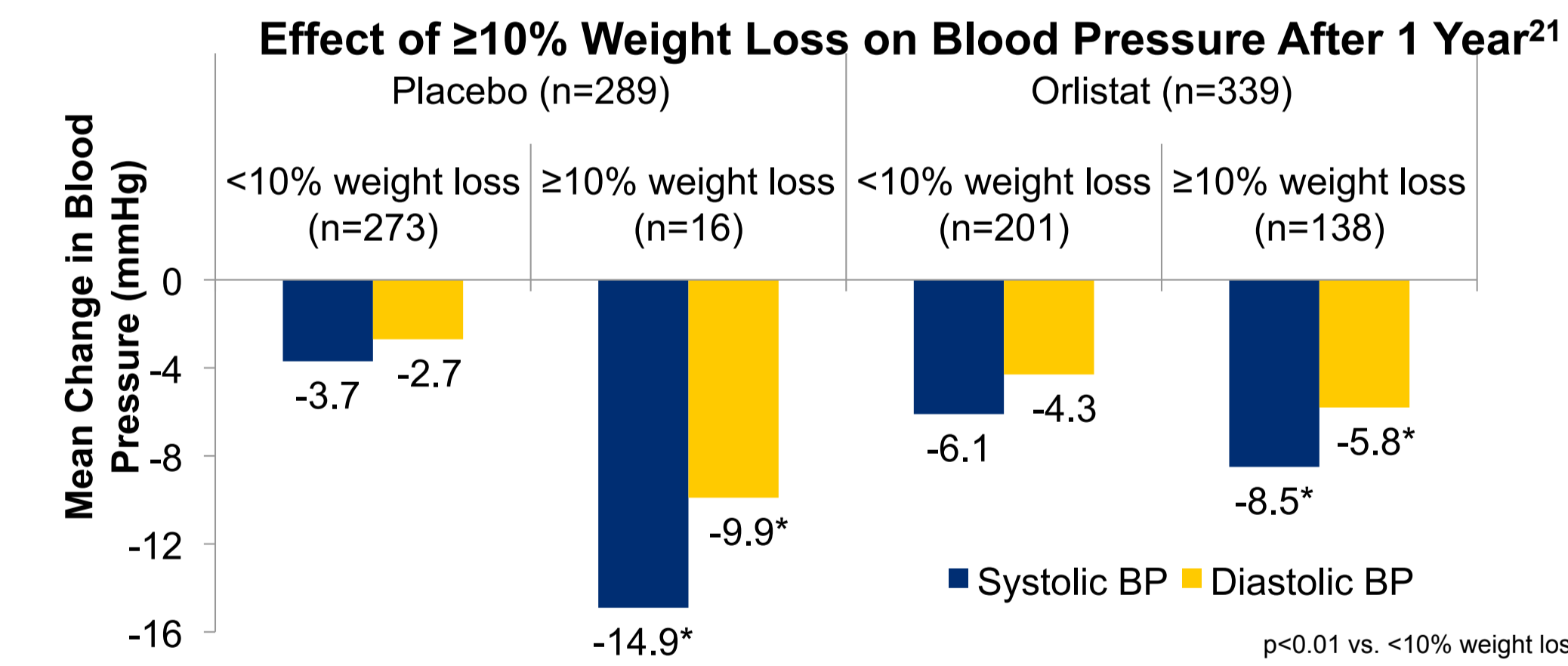


## RESULTS: EFFECT OF ≥10% WEIGHT LOSS ON CARDIOMETABOLIC RISK FACTORS

Study	Duration	Weight Loss	Lipids				Glycemic Markers			Vascular Inflammation Markers			
			TG	HDL-C	TC	LDL-C	FBG	Insulin	HOMA	CRP	TNF-α	IL-6	Adiponectin
Coppola, 2009 <sup>8</sup>	1 year	≥10%	—	—	—	—	-9.6%	-35.7%	-40.6%	-40%†	—	—	58.8%‡
Dandona, 1998 <sup>9</sup>	1 year	Mean 12.3%	—	—	—	—	—	—	—	—	-23.8%*	—	—
Ditschuneit, 1999 <sup>10</sup>	27 months	Mean 11.3%	-37.2%†	6.1%	-8.2%†	—	-11.5%†	-38.0%†	—	—	—	—	—
Esposito, 2003 <sup>11</sup>	2 years	Mean 14.7%	-13.4%*	17.4%*	-2.0%*	—	-8.5%†	-35.7%*	-36.1%*	-34.4%†	—	-32.6%†	48.2%*
Esposito, 2004 <sup>12</sup>	2 years	Mean 14.6%	-12.0%†	8.9%†	-5.8%†	—	—	-36.4%†	-48.0%‡	-42.4%†	—	-50.0%*	—
Fleming, 2002 <sup>13</sup>	1 year	Mean 12.6%	-36.9%†	3.6%	-30.4%§	-38.8%§	—	—	—	—	—	—	—
Madsen, 2008 <sup>14</sup>	3 years	≥11%	-32.7%†	10.4%*	-8.9%	-9.2%	—	—	-59.0%‡	—	—	—	—
Marfella, 2004 <sup>15</sup>	1 year	≥10%	—	—	—	—	-7.3%*	-34.5%*	-38.9%*	-44.1%*	-31.0%†	-61.9%†	—
McNulty, 2003 <sup>5</sup>	1 year	≥10%	-29.0%†	10.0%	—	—	-19.1%‡	—	—	—	—	—	—
Nicoletti, 2003 <sup>16</sup>	1 year	≥10%	—	—	—	—	—	—	—	—	-29.1%†	—	—
Poitou, 2006 <sup>17</sup>	1 year	Mean 18.8%	-7.4%§	40.5%†	5.6%	—	-8.5%†	-15.9%§	—	-24.6%§	0.3%	-8.9%§	57.0%§
Tchemof, 2002 <sup>18</sup>	14 months	Mean 14.5%	-15.0%	60.6%§	5.0%	-2.9%	—	—	—	-32.3%§	—	—	—
Sjostrom, 2004 <sup>6</sup>	10 years	Mean 16.1%	-16.3%‡	24.0%‡	-6.0%*	—	-2.5%‡	-28.2%‡	—	—	—	—	—
Wadden, 1999 <sup>9</sup>	2 years	≥10%	-34.8%*	-3.2%	-12.1%*	-11.0%*	—	—	—	—	—	—	—
Wadden, 2005 <sup>19</sup>	1 year	Mean 11.1%	-26.7%†	4.7%	-4.0%	—	-3.2%	-8.9%	—	—	—	—	—
Wing, 1987 <sup>4</sup>	1 year	Mean 10%	-20.5%†	6.4%*	—	—	-15.1%*	-42.3%†	—	—	—	—	—
Ziccarda, 2002 <sup>20</sup>	1 year	≥10%	—	—	—	—	-6.3%*	-22.2%*	—	—	-31.0%†	-46.5%†	—

<sup>†</sup>p<0.05, <sup>‡</sup>p<0.01, <sup>§</sup>p<0.001, <sup>§§</sup>p<0.0001  
 CRP=C-reactive protein; FBG=fasting blood glucose; HbA1c=glycosylated hemoglobin; HDL-C=high-density lipoprotein cholesterol; HOMA-IR=homeostatic model assessment of insulin resistance; IL=interleukin; LDL-C=low-density lipoprotein cholesterol; TC=total cholesterol; TG=triglycerides; TNF=tumor necrosis factor

## RESULTS: EFFECT OF ≥10% WEIGHT LOSS ON BLOOD PRESSURE



## RESULTS: WEIGHT LOSS & MORTALITY

- In a longitudinal study of 4,970 overweight persons with diabetes, intentional weight loss (mean weight loss of 11%) was associated with a 25% reduced risk of all-cause mortality (RR=0.75; 95% CI 0.67-0.84) and a 28% reduction in CVD and diabetes mortality (RR=0.72; 95% CI 0.63-0.82).<sup>22</sup>
- Individuals who lost 10-15% of weight (20-29 lbs.) had the largest reduction in mortality (33%) (RR=0.67; 95% CI 0.58-0.77).

## CONCLUSIONS

- Although some long-term studies, such as the Diabetes Prevention Program (DPP),<sup>23</sup> have demonstrated that a 5-10% weight loss can yield substantial reductions in obesity-related risks, sustained weight loss of ≥5% has not been consistently associated with improvements in cardiovascular risk factors.<sup>24</sup>
- Evidence presented in this review indicates that the greatest and most consistent improvements in obesity-related risk factors are associated with ≥10% versus <10% weight loss.
- It also appears that 10-20% weight loss yields the maximal effect on lipid levels in patients with morbid obesity at 12-18 months of follow-up, and that more pronounced weight loss does not additively improve the lipid profile.<sup>25</sup>
- There is a need for more research that directly assesses the relationship between magnitude of weight loss and long-term health benefits for obese/overweight persons.
- Such research, along with available evidence, should inform coverage and reimbursement decisions about weight loss treatments.

## REFERENCES

See handout for list of references.

## FOR FURTHER INFORMATION

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## DISCLOSURES

Cheryl Hankin and Amy Bronstone are consultants to VIVUS, Inc. Research supported by VIVUS, Inc.