

# Medically Safe Rate of Weight Loss for the Treatment of Obesity: A Guideline Based on Risk of Gallstone Formation

Roland L. Weinsier, MD, DrPH, Louis J. Wilson, MD, Jeannette Lee, PhD, Birmingham, Alabama

**OBJECTIVE:** Currently recommended rates of weight loss for obese persons are not based on demonstrated health risks. The authors attempt to determine a medically safe rate of weight loss based on currently available data on the risk of gallstone formation during active weight loss.

**METHODS:** All prospective studies published in the English language on the formation of gallstones in obese persons during active weight loss were reviewed and evaluated. A statistical analysis was performed using studies of at least 4 weeks' duration that included information on diet composition, rates of weight loss, length of follow-up, and incidence of gallstone formation. A statistical model was fit to the data from the studies that met the criteria.

**RESULTS:** Nine subject groups derived from five published reports met the criteria for inclusion in the analysis. When the results of these groups were evaluated statistically, a curvilinear relationship between incidence of gallstone formation and rate of weight loss was demonstrated. The relationship was best described by an exponential regression curve, with an adjusted  $r^2$  of 0.98 and a dramatically increasing risk of gallstone formation at rates of weight loss above 1.5 kg per week.

**CONCLUSION:** Risk of gallstone formation in obese persons during active weight loss seems to increase in an exponential fashion. The data suggest that rates of weight loss should not exceed an average of 1.5 kg per week.

Over the past decade, a number of organizations have published guidelines for safe rates of weight loss for obese individuals. These include the Canadian Task Force on the Treatment of Obesity in 1991,<sup>1</sup> The Michigan Task Force to Establish Weight Loss Guidelines in 1990,<sup>2</sup> and The International Congress on Obesity in 1984.<sup>3</sup> The recommendations from these groups range from 1 kg per week, or 1% of body weight

per week, to 1.5 kg per week; however, with the available evidence, it is difficult to define a threshold rate of weight loss below which health risk is low. In fact, there are no studies published that quantify the relationship between rate of weight loss and an objective measure of morbidity.

Among the postulated health risks, only the formation of gallstones seems to be of substantial concern; therefore, conclusions about safe rates of weight loss seem to depend mostly on this factor.<sup>4,5</sup> This brief study will use the available prospective data to recommend a rate of weight loss that seems to be associated with a relatively low risk of gallstone formation.

## METHODS

All studies concerning gallbladder function, gallstone formation, and weight loss in obese persons published in the English language from 1970 to 1993 were identified using *Index Medicus*, and the bibliographies of these studies were then searched for papers that were possibly missed. Studies involving bariatric surgery were eliminated.

In forming the inclusion criteria for this analysis, various concerns arose. Since it appears from the literature that at least 4 weeks is required for gallstone formation during dieting, studies of less than 4 weeks' duration were excluded from the analysis. Also, a number of publications addressed the issue of weight loss and gallstone formation; however, only a few provided the type of information needed to make a recommendation about a safe rate of weight loss for obese persons. Thus, it was felt that the criteria necessary for inclusion in this analysis must include data on diet composition, rates of weight loss, length of treatment, and incidence of new gallstone formation. New gallstone formation during weight loss was defined as the appearance of previously absent gallstones by ultrasound examination. Only five studies met all inclusion criteria.<sup>6-10</sup>

For the statistical analysis, distinct observation groups were obtained from each study. When more than 1 group was identified within a published report, each group was considered as an individual observation group for this analysis: Liddle et al<sup>7</sup> divided the subjects in their study into a control group and a weight loss group, and Yang et al<sup>6</sup> divided the subjects in their study into 4 groups (quartiles) based on the subjects' rate of weight loss. Thus, a total of 9 observation groups from five studies were included in the analysis, the characteristics of which are sum-

From the Departments of Nutrition Sciences (RW) and Medicine (LJW), and the Biostatistics Unit (JL), Comprehensive Care Center, University of Alabama at Birmingham, Birmingham, Alabama.

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Requests for reprints should be addressed to Roland L. Weinsier, MD, Department of Nutrition Sciences, University of Alabama at Birmingham, Birmingham, Alabama 35294-3360.

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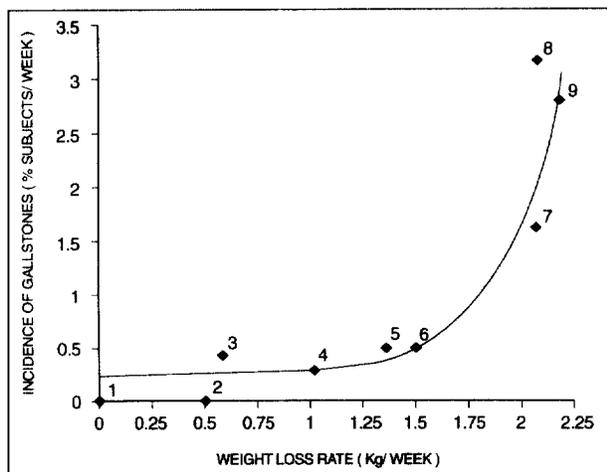
TABLE

**Characteristics of the Observational Groups Derived From  
Published Studies of Gallstone Formation During Weight Loss in Obese Persons**

Observation Group	Number of Subjects	Duration of Intervention (wk)	Rate of Weight Loss (kg/wk)	Incidence of Gallstones (% subjects/wk)	Reference #
1	26	8	0	0	7 (controls)
2	17	11*	0.5	0	10
3	61	16	0.6	0.4	6 (1st quartile)
4	68	16	1.0	0.3	6 (2nd quartile)
5	58	16	1.4	0.5	6 (3rd quartile)
6	38	10	1.5	0.5	9
7	50	16	2.1	1.6	6 (4th quartile)
8	51	8	2.1	3.2	7
9	19	9.5*	2.2	2.7	8 (placebo) <sup>†</sup>

\*Average reported dietary intervention.

<sup>†</sup>This study group received placebo versus medication to prevent gallstone formation.



**Figure.** The relationship of incidence of gallstone formation to rate of weight loss in obese persons based upon published studies. The numbers in the figure correspond to the observation groups listed in the Table.

marized in the **Table**.

Among the studies, all except Hoy et al<sup>9</sup> and Nunez et al<sup>10</sup> reported initial average body weights. For those reported, the weights ranged from 99 to 106 kg, with a mean of 101 kg. For each observation group, the rate of weight loss (kg/wk) and incidence of gallstones (percent of subjects/wk) were calculated. Finally, the data were weighted based on the number of subjects in each group, and a best-fit regression curve was fitted to the data.

## RESULTS

The model that best fits the data is graphically displayed in the **Figure** and is represented by the general equation:

Incidence = Constant + Coefficient exp ( $X^2$ ),  
in which X is the rate of weight loss (kg/wk) and incidence is the percent of subjects per week developing gallstones. Specifically this is:

$$\text{Incidence} = 0.199 + 0.021 \exp (X^2).$$

The  $r^2 = 0.98$ . Thus, using this equation, 98% of the variability in incidence of gallstone formation can be explained by the rate of weight loss. The data indicate that the incidence of gallstone formation is essentially unchanged below rates of 1.5 kg/wk.

## DISCUSSION

It appears from this analysis that the risk of new cholelithiasis during dieting rises exponentially with increasing rates of weight loss. Furthermore, the regression curve suggests that rates of weight loss above 1.5 kg/wk are associated with dramatically higher rates of gallstone formation than rates below 1.5 kg/wk. In obese persons whose initial body weight averages 100 kg, this would translate to a 1.5% loss of body weight per week.

There are a number of limitations to using this statistical analysis to support a recommendation for a safe rate of weight loss for obese persons. Subject characteristics may be variable, such as age and sex, and these may affect susceptibility to gallstone formation.<sup>11,12</sup> The potential effects of comorbid conditions, such as insulin resistance and hyperlipidemia, which could function as motivating factors for faster rates of weight loss, are difficult to define without larger prospective studies. Also, diet composition among the studies is not uniform. Furthermore, since none of the studies extended beyond 16 weeks, the relationship beyond that time cannot be predicted; however, it is reasonable to assume that risk would be attenuated. If this were not the case, the subjects of Liddle et al,<sup>7</sup> for instance, who developed gallstones at a rate of 3.2% per week, would have the unlikely occurrence rate of 100% at the end of 31 weeks of dieting. Despite these limitations, this analysis reveals a surprisingly consistent relationship among the studies between rate of weight loss and formation of gallstones.

It has been suggested that the fat content of the weight-reducing diet may be responsible for the de-

velopment of cholelithiasis rather than the rate of weight loss per se.<sup>13</sup> However, among the studies used in this analysis, fat content did not appear to affect the relationship between rate of weight loss and gallstone formation. Six of the data points represent studies using diets of very low fat content (ie, <1 g fat/d), whereas the study by Hoy et al<sup>9</sup> used a diet containing 13 to 23 g fat/d and the control group of Liddle et al<sup>7</sup> had ad libitum intake of fat. Despite a diet with a much lower fat content, the third quartile group from the study by Yang et al<sup>6</sup> had a similar rate of weight loss and rate of gallstone formation as the group from the study by Hoy et al.<sup>9</sup> This suggests that rate of weight loss or degree of energy restriction, and not fat content, was the important factor.

## CONCLUSION

This analysis provides objective data to support the currently published guidelines for the treatment of obesity. Although the findings cannot be used to predict the risk of gallstone formation during weight loss for a particular patient, clinicians should counsel their patients that average rates of weight loss over 1.5 kg/wk will increase this risk. Pending the availability of large-scale, prospective trials to define all the health risks of rapid weight loss, an average of 1.5 kg/wk should be considered an upper limit for medically safe weight loss.

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