

Listed below are the average weight changes for sub-group II. Both male and female data are included.

SUBGROUP II.—AVERAGE WEIGHT CHANGES

[In pounds]

Table	Duration (weeks)	Placebo	40 mg	60 mg
C.....	2	-1.94 24/24	-1.86 23/23	-3.63 49/50
D.....	4	-1.88 19/24	-4.31 22/23	-5.57 44/50
E.....	6	-1.67 19/24	-6.52 19/23	-6.37 47/50

Four studies contributed to these larger study numbers. The data are predominantly those of females; only seven males provided data. The weight losses again appear to be dosage related and may be affecting some of the bias in Tables A and B on initial body weight and percent overweight.

The weight losses in the drug group appear to be more consistent and larger than those of subgroup I. Even the placebo managed to provide some "anorexic" effect over the 6 weeks' period.

Shown below are the data for sub-group III. Males and females have been combined.

Average change in body weight (pounds)

Table and duration	Placebo	60 mg
Subgroup III:		
C—2 weeks.....	-1.10 56/57	-3.17 73/78
D—4 weeks.....	-1.11 42/57	-4.91 66/78
E—6 weeks.....	1.52 30/57	-5.88 55/78

Seven studies contributed data to this tabulation. It provides the strongest base for comparing placebo with a drug group—in this instance, the 60 mg/day dosage. The advantage over placebo appears substantial and seems to increase with study length. However, there are at three factors which must be taken into account in judging this relative advantage.

1. The placebo has provided some weight loss or "anorexic" effect in all sub-groups and study periods. Therefore, there is a built-in placebo effect component in the drug average.

2. The initial baseline imbalances and biases must be contributing to some extent to the weight loss of the drug group.

3. At least four of the studies had twice as many subjects assigned to the 60 mg group than to placebo. This suggests that these studies may not have been blind and well controlled and that subjectivity may well have influenced the recording of weight loss data.

Just how much the above and other factors contributed to the greater weight loss and just how much was contributed by the drug ingredients is not known. This puts us in a difficult situation because we see some evidence of effectiveness but it is based on relatively insufficient and to some extent questionable evidence. Furthermore, the data submitted suggest a lessening effectiveness with duration of drug use.

The data submitted by the firm and also re-tabulated into my sub-groups should be evaluated on a weekly loss basis to be fully meaningful. When this is done for sub-group III data for example, the weekly weight losses do have a trend.

SUBGROUP III.—AVERAGE WEEKLY CHANGE IN BODY WEIGHT

[In pounds]

Table	Duration (weeks)	Placebo	60 mg
C.....	2	-0.55	-1.58
D.....	4	-.28	-1.23
E.....	6	-.25	-.98