

these summary tables. Please note that in these four studies twice as many subjects were given the 60 mg dosage. This suggests a predetermined clinical emphasis or bias in the allocation of study material to the treatments used.

Seven studies provided 135 subjects with which to compare placebo and the 60 mg dosage. Again, these are maximum counts and are not always represented by data in the tables. The average number of subjects per study is only 8 for placebo and 11 for the drug.

I have recomputed all tables (A, B, C, etc) for these three sub-groups. In tables A and B, the bias and trends with increasing dosage of initial body weights and percent overweight appear to persist in all three sub-groups. The averages for each study group are shown below. The numbers in parentheses represent the number of subjects contributing data to these averages. Sexes are combined.

TABLE A.—AVERAGE INITIAL BODY WEIGHT

Subgroup	Placebo	49 mg	60 mg	120 mg
I.....	191 (17)		186 (15)	208 (16)
II.....	175 (24)	182 (23)	189 (50)	
III.....	176 (57)		186 (78)	

Study number 12 (Fred), included in both II and III, was particularly biased against placebo. Initial weights in the order above were 152, 181, 190.

TABLE B.—AVERAGE INITIAL PERCENT OVERWEIGHT

Subgroup	Placebo	40 mg	60 mg	120 mg—
I.....	56 (4)		30 (3)	64 (3)
II.....	38 (23)	36 (23)	50 (50)	
III.....	36 (43)		45 (62)	

Only nine females provided data for group I and these counts are too small for judging trends. These data also show a considerable bias against placebo in study 12 for which percent overweights averages were 22, 37 and 53, respectively, for the placebo, 40 mg and 60 mg groups.

Presented below are summary data for sub-group I corresponding to Tables C, D, and E. The fraction to the right of the average weight changes indicates the ratio of the numbers of subjects providing data to that in the population studied. For example in the two weeks' data, twelve of seventeen placebo patients had weight measurements at the two week interval and thus provided data for the average—0.66 pounds reduction. The numerators vary considerably for each study interval and strengthens our concern about small and spotty sample sizes.

Table and study duration	Average weight change (pounds)		
	Placebo	60 mg	120 mg
Subgroup I:			
C—2 weeks.....	-0.66 12/17	-2.00 9/15	-2.92 10/16
D—4 weeks.....	-.93 7/17	-2.90 10/15	-7.12 8/16
E—6 weeks.....	-2.58 11/17	-3.00 8/15	-2.67 3/16

The above averages provide a suggestion of efficacy that appears to be dose related as are the data in Tables A and B. What appeared to be a strong advantage for the 120 mg dosage seems to be washed out at the 6th week interval. To emphasize the uncertainties in these averages, it should be pointed out that a single placebo subject provided a weight loss which was responsible for most of the increase in the placebo average at the 6th week. This patient was not included in the data for the second and fourth week averages. Also, a single subject was responsible for the large 120 mg average at the 4th week; this subject was not included in the data for the other two averages.