CASE STUDY 21.1 Premenstrual Syndrome? Try Calcium

It was front page news in the *Sacramento Bee.* The headline read "Study says calcium can help ease PMS," and the article continued: "Daily doses of calcium can reduce both the physical and psychological symptoms of premenstrual syndrome by at least half, according to new research that points toward a low-cost, simple remedy for a condition that affects millions of women" (Maugh, 26 August 1998). The article described a randomized, double-blind experiment in which women who suffered from premenstrual syndrome (PMS) were randomly assigned to take either a placebo or 1200 mg of calcium per day in the form of four Tums E-X tablets (Thys-Jacobs et al., 1998). Participants included 466 women with a history of PMS: 231 in the calcium treatment group and 235 in the placebo group.

The primary measure of interest was a composite score based on 17 PMS symptoms, including six that were mood-related, five involving water retention, two involving food cravings, three related to pain, and insomnia. Participants were asked to rate each of the 17 symptoms daily on a scale from 0 (absent) to 3 (severe). A composite "symptom complex score" was created by using the mean rating for the 17 symptoms. Thus, a score of 0 would imply that all symptoms were absent, and a score of 3 would indicate that all symptoms were severe. The original article (Thys-Jacobs et al., 1998) presents results individually for each of the 17 symptoms plus the composite score.

One interesting outcome of this study was that the severity of symptoms was substantially reduced for both the placebo and the calcium-treated groups. Therefore, comparisons should be made between those two groups rather than examining the reduction in scores before and after taking calcium for the treatment group alone. In other words, part of the total reduction in symptoms for the calcium-treated group could be the result of a "placebo effect." We are interested in knowing the additional influence of taking calcium.

Let's compare the severity of symptoms as measured by the composite score for the placebo and calcium-treated groups. The treatments were continued for three menstrual cycles; we report the symptom scores for the premenstrual period (7 days) before treatments began (baseline) and before the third cycle.

Table 21.3 presents results as given in the journal article, including sample sizes and the mean symptom complex scores ± 1 standard deviation. Notice that sample sizes were slightly reduced by the third cycle due to patients dropping out of the study. Let's use the results in the table to compute a confidence interval for what the mean differences would be for the entire population of PMS sufferers.

The purpose of the experiment is to see if taking calcium diminishes symptom severity. Because we know that placebos alone can be responsible for reducing symptoms, the appropriate comparison is between the placebo and calcium-treated

TABLE 21.3 Results for Case Study 21.1

	Symptom Complex Score: Mean ± *SD*	
	Placebo Group	**Calcium-Treated Group**
Baseline	0.92 ± 0.55 ($n = 235$)	0.90 ± 0.52 ($n = 231$)
Third cycle	0.60 ± 0.52 ($n = 228$)	0.43 ± 0.40 ($n = 212$)

groups rather than between the baseline and third cycle symptoms for the calcium-treated group alone.

The difference in means (placebo − calcium) for the third cycle is $(0.60 - 0.43) = 0.17$. The "standard error" is about 0.039, so a 95% confidence interval for the difference is $0.17 \pm 2(0.039)$, or about 0.09 to 0.25.

To put this in perspective, remember that the scores are averages over the 17 symptoms. Therefore, a reduction from a mean of 0.60 to a mean of 0.43 would, for instance, correspond to a reduction from $(0.6)(17) = 10$ mild symptoms (rating of 1) to $(0.43)(17) = 7.31$, or just over seven mild symptoms. In fact, examination of the full results shows that all 17 symptoms had reduced severity in the calcium-treated group compared with the placebo group. And, because this is a randomized experiment and not an observational study, we can conclude that the calcium actually *caused* the reduction in symptoms.

As a final note, Table 21.3 also indicates a striking drop in the mean symptom score from baseline to the third cycle for both groups. For the placebo group, the symptom scores dropped by about a third; for the calcium-treated group, they were more than cut in half. Thus, it appears that placebos can help reduce the severity of PMS symptoms. ■