

Annals of Internal Medicine

Gastrointestinal Symptoms in 3181 Volunteers Ingesting Snack Foods Containing Olestra or Triglycerides

A 6-Week Randomized, Placebo-Controlled Trial

Robert S. Sandler, MD, MPH; Nora L. Zorich, MD, PhD; Thomas G. Filloon, PhD; Heather B. Wiseman; Dennis J. Lietz, BBA; Michael H. Brock, MS; Mary G. Royer, MS; and Robert K. Miday, MD

Background: Olestra is a nonabsorbable, energy-free fat substitute. Because it is not absorbed, it may cause digestive symptoms when consumed in large amounts.

Objective: To compare the frequency and impact of gastrointestinal symptoms in adults and children who freely consume snacks containing olestra or regular snacks in the home.

Design: 6-week, double-blind, randomized, parallel, placebo-controlled trial.

Setting: General community.

Participants: 3181 volunteers 2 to 89 years of age.

Intervention: Households received identical packages labeled as containing olestra corn or potato chips. These packages contained either olestra or regular chips (control).

Measurement: Gastrointestinal symptoms and their impact on daily activities were reported in a daily record.

Results: At least one gastrointestinal symptom was reported by 619 of 1620 (38.2%) persons in the olestra group and 576 of 1561 (36.9%) controls (difference, 1.3 percentage points [95% CI, -3.6 to 6.2 percentage points]; $P = 0.60$). In general, the groups did not differ significantly in the proportion of participants who reported individual gastrointestinal symptoms; however, more controls reported nausea (8.4% compared with 5.7%; difference, -2.7 percentage points [CI, -4.9 to -0.4 percentage points]; $P = 0.02$). The only difference between groups for the mean numbers of days on which symptoms were reported was that participants in the olestra group had 1 more symptom-day of more frequent bowel movements than did controls (3.7 symptom-days compared with 2.8 symptom days; difference, 0.9 symptom-days [CI, 0.1 to 1.8 symptom-days]; $P = 0.04$). The groups did not differ in the impact of symptoms on daily activities.

Conclusions: Clinically meaningful or bothersome gastrointestinal effects are not associated with unregulated consumption of olestra corn and potato chips in the home.

Olestra is an energy-free fat substitute approved by the U.S. Food and Drug Administration for use in snack foods, including potato chips, corn chips, and crackers (1). Olestra, a mixture of sucrose esters of long-chain fatty acids isolated from edible fats and oils, is neither digested nor absorbed (2, 3).

Anecdotal reports of severe diarrhea and abdominal pain associated with ingestion of olestra (4) have not been substantiated by extensive controlled testing (5-7). A recent large study, in which participants ate chips at a single sitting, showed no differences in gastrointestinal symptoms between participants who ate olestra chips and those who ate regular chips (8). We wanted to obtain data from a larger sample that freely consumed olestra snacks over a longer period. We therefore conducted a randomized, double-blind, placebo-controlled trial to evaluate the frequency of gastrointestinal symptoms and their impact on daily living in a diverse, free-living study sample consuming olestra chips over a 6-week period under market use conditions in the home environment.

Methods

The study was conducted in Phoenix, Arizona, and St. Petersburg, Florida, from 28 July 1997 to 22 September 1997. The protocol was approved by the institutional review board of Hill Top Research, Inc., Cincinnati, Ohio.

This paper is also available at <http://www.acponline.org>.

Ann Intern Med. 1999;130:253-261.

See editorial comment on pp 320-322.

Participants

Participants were recruited by telephone from rosters of participants in previous consumer product studies or from print advertising in Phoenix and St. Petersburg. Persons 2 years of age or older were eligible for participation. For households to be eligible, at least half of their members had to have eaten corn or potato chips 4 or more times in the past month, and all eligible members had to participate. Persons were excluded if medical reasons precluded them from eating regular potato or corn chips.

At the initial visit, each household was assigned to the olestra or control group by means of a separate computer-generated randomization schedule for each of four strata (households with or without children 2 to 12 years of age at each of the two sites) (S-Plus, version 3.3, MathSoft, Inc., Seattle, Washington). Because the unit of randomization was the household, all members of the same household received the same study treatment. An adult "household contact" was designated to return to the study site each week (within a period of 7 ± 2 days) for 6 consecutive weeks.

Products

At each visit, household contacts viewed a display of 14 olestra-labeled and regular (full-fat) potato and corn chips and ordered up to 8 packages in any combination of olestra or regular packages. The olestra-labeled packages provided to households in the olestra group contained olestra (Olean, Procter & Gamble, Cincinnati, Ohio) products, but the olestra-labeled packages provided to households in the control group actually contained regular (control) chips. Households in both groups could also select regular chips in marketed packages.

The olestra products consisted of seasoned and plain olestra potato chips (WOW brand Lays and Ruffles, Frito-Lay, Dallas, Texas), corn chips (WOW brand Doritos, Frito-Lay), and potato crisps (Pringles Fat-Free brand, Procter & Gamble). The matching control products consisted of seasoned and plain regular potato chips (Lays and Ruffles, Frito-Lay), corn chips (Doritos, Frito-Lay), and potato crisps (Pringles, Procter & Gamble). All of the products were regular commercial products obtained from the manufacturers and were distributed free of charge in 5.5- to 9-ounce standard market packages.

The olestra-labeled packages containing olestra snacks were identical in appearance to the olestra-labeled packages containing regular snacks. Each package displayed the Olean logo and the following information statement: "This Product Contains Olestra. Olestra may cause abdominal cramping and loose stools. Olestra inhibits the absorption of some

vitamins and other nutrients. Vitamins A, D, E and K have been added."

Participants were instructed to eat the chips as they normally would. They were also told not to share the chips outside of the household and not to consume any chips other than those provided at the study site.

All study participants and personnel associated with the collection, processing, or analysis of the data were blinded to study group assignment. They were also blinded to the type of study product contained in olestra-labeled packages. Product orders were filled by staff who were specifically assigned to that duty and had no contact with the study participants. The randomization code was not available to the persons conducting the study.

Study Procedures and Data Collection

Before the study started, a screening telephone call was made to each household to determine interest in and eligibility for participation in the study. All household members who agreed to participate came to the study site for the initial visit. At this time, information collected during the screening phone call was verified, medical histories were recorded, and written informed consent was obtained from all participants or their guardians. The informed consent form explained to the participants that the olestra-labeled packages they selected might contain olestra chips or regular full-fat chips. The form also stated that "During this study, as with other changes in the diet or eating habits, some individuals may notice digestive changes or discomfort such as cramping or loose stools." Participants viewed a video instructing them how to complete the study records.

During the study, all participants indicated on a daily record how much of the olestra-labeled and regular chips they ate, in increments of one quarter of a package, and whether they had any digestive symptoms. The household contact assisted children or completed the daily records for them, as needed. Participants noted whether they experienced any of the following symptoms: heartburn or indigestion, nausea or queasiness, vomiting, gas, bloating, abdominal cramping or pain, more frequent bowel movements, or looser stool or other digestive symptoms. Participants indicated how the symptoms affected their daily activities by checking one of the following categories: 1) noticed symptoms but did not affect activities, 2) symptoms slightly affected activities, 3) missed some time at activities, or 4) missed all day at activities. Participants also noted whether they took medication or visited a physician because of their symptoms. At the end of the study, participants indicated which snacks they thought they had eaten (olestra, regular, or didn't know).

Study personnel reviewed the daily records for accuracy and completeness in the presence of the participant at each weekly visit. Although the amount of chips consumed in this study was not objectively verified, we conducted a pretrial 6-week pilot study to confirm that the data collected in the daily record would be representative of actual chip consumption. In that study, 70% of consumption estimates were within 30% of the actual weight of the chips consumed.

Statistical Analysis

The study was designed to provide at least 80% power (at an α level of 0.05) for detecting true differences between groups of 6% to 8% in the proportions of participants with symptoms, based on 500 households per test group. To account for the possible correlation of within-household information, variance estimation was done by using the sampling theory approach for ratio estimates, as described elsewhere (9, 10). Testing for treatment differences was then done by using the normal approximation method. All *P* values are two-sided and were not adjusted for multiple comparisons. Approximate 95% CIs for the difference between two proportions were constructed by using the standard large-sample normal approximation method. All statistical analyses were performed by using S-Plus software, version 3.3 (MathSoft, Inc.)

Role of the Funding Source

Data were collected by an independent contractor (Hill Top Research, Inc., Cincinnati, Ohio). Analyses were performed by the sponsor, and the results were submitted to the U.S. Food and Drug

Table 1. Demographic Characteristics of Study Participants*

Characteristic	Olestra Group (n = 1620)	Control Group (n = 1561)	All Participants (n = 3181)
	←-----n (%)-----→		
Age			
2–12 years	442 (27.3)	443 (28.4)	885 (27.8)
13–17 years	125 (7.7)	102 (6.5)	227 (7.1)
18–64 years	842 (51.9)	825 (52.9)	1667 (52.4)
65–89 years	211 (13.0)	191 (12.2)	402 (12.6)
Sex			
Male	696 (43.0)	704 (45.1)	1400 (44.0)
Female	924 (57.0)	857 (54.9)	1781 (56.0)
Ethnicity			
White	1429 (88.2)	1394 (89.3)	2823 (88.7)
African-American	71 (4.4)	81 (5.2)	152 (4.8)
Hispanic	84 (5.2)	63 (4.0)	147 (4.6)
Asian	14 (0.9)	2 (0.1)	16 (0.5)
Native American	9 (0.6)	13 (0.8)	22 (0.7)
Other	13 (0.8)	8 (0.5)	21 (0.7)
Highest level of education reached†			
High school (grade 12) or less	211 (37.5)	212 (37.4)	423 (37.4)
More than high school	353 (62.5)	355 (62.6)	707 (62.5)
Median yearly household income‡			
≤\$35 000	335 (59.5)	347 (61.3)	682 (60.4)
>\$35 000	180 (32.0)	170 (30.0)	350 (31.0)
Did not state	48 (8.5)	49 (8.7)	97 (8.6)

* Includes participants who ate olestra-labeled corn or potato chips at least once.

† Information on education was collected for the household's main wage earner only.

‡ Information was available for 563 participants in the olestra group and 566 participants in the control group.

Administration for review. The principal investigator had final authority with respect to publication of results.

Results

Disposition and Demographic Characteristics of the Study Participants

A total of 3250 volunteers—1651 persons from 579 households in the olestra group and 1599 persons from 581 households in the control group—were randomly allocated (Figure). Of these, 24 volunteers (14 in the olestra group and 10 in the control group) were excluded because they did not eat olestra-labeled chips. Of the 130 volunteers who withdrew from the study, 45 (17 in the olestra group and 28 in the control group) did so before the second visit and did not return any daily records. Therefore, 3181 volunteers, including 885 children 2 to 12 years of age and 402 elderly persons 65 to 89 years of age, were included in the analysis. Data from the 85 participants who withdrew after the second visit were included in the analysis up to the time of discontinuation.

Participants in the olestra and control groups were similar with respect to age, sex, and ethnicity ($P > 0.2$) (Table 1). They were also similar in terms

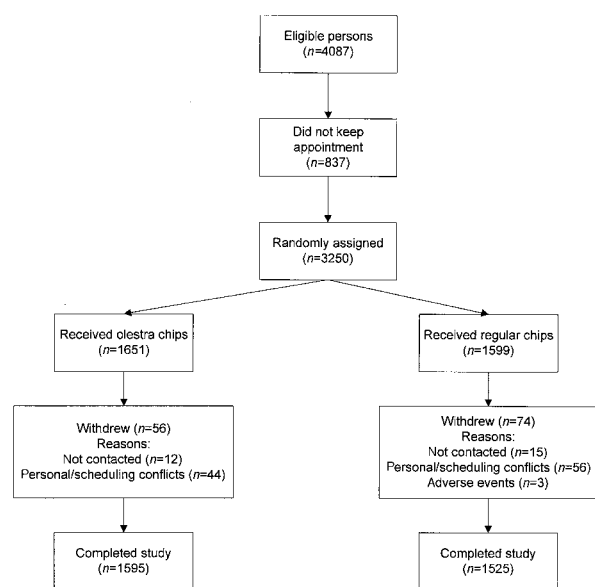


Figure. Progress of study participants during randomization and during the trial.

Table 2. Consumption of Olestra-Labeled Chips

Consumption Data	Olestra Group				Control Group			
	Participants	Eating Days*			Participants	Eating Days*		
		Median	25th, 75th Percentile	90th Percentile		Median	25th, 75th Percentile	90th Percentile
	<i>n</i>	<i>d</i>			<i>n</i>	<i>d</i>		
Overall	1620	20	12, 28	35	1561	21	14, 29	36
Men	696	18	11, 26	34	704	19	13, 27	36
Women	924	21	14, 29	35	857	22	15, 31	37
Children (2–12 years of age)	442	18	11, 24	32	443	18	12, 25	32
Teenagers (13–17 years of age)	125	15	10, 24	28	102	18	12, 23	31
Adults (18–64 years of age)	842	20	13, 28	34	825	21	15, 29	35
Seniors (65–89 years of age)	211	27	19, 35	40	191	32	21, 36	40

* Number of days on which olestra-labeled chips were eaten.

† The average amount of chips eaten per eating day is defined as the amount of chips eaten by a participant divided by his or her number of eating days.

of highest level of education reached, occupation of the main wage earner, and yearly household income.

Consumption of Study Product

During the 42-day study, participants in both groups ate olestra-labeled chips frequently (**Table 2**). Although consumption was slightly lower in the olestra group than in the control group, olestra chips were consumed on approximately half of the study days in a median daily amount of more than 1 ounce. In both groups, the weekly percentages of participants consuming olestra-labeled chips were consistent (82% to 91% in the olestra group and 88% to 92% in the control group) and showed no trends throughout the study. The median number of eating days and the total amount of olestra-labeled chips eaten were greatest among elderly participants. Men ate more olestra-labeled chips per eating day than women, but women tended to eat olestra-labeled chips more frequently than men and, as a result, consumed a greater median total amount. The median total amount eaten by children was about 25% less than that eaten by the group as a whole.

Symptoms

Analysis of the frequency of gastrointestinal events showed no statistically significant differences between the proportions of participants in the olestra and control groups who reported any gastrointestinal symptom (619 of 1620 [38.2%] persons in the olestra group and 576 of 1561 [36.9%] controls; difference, 1.3 percentage points [95% CI, -3.6 to 6.2 percentage points]; $P > 0.2$) (**Table 3**). In general, the test groups did not differ significantly in the proportion of participants reporting any of the eight individual gastrointestinal symptoms, except that a higher percentage of controls reported nausea (5.7% compared with 8.4%; difference, -2.7 percentage points [CI, -4.9 to -0.4 percentage points]; $P = 0.02$).

For participants reporting gastrointestinal symptoms, the groups did not generally differ in the number of days that symptoms were reported (symptom-days) for any gastrointestinal symptom or for any of the eight individual gastrointestinal symptoms; however, participants in the olestra group had 1 more symptom-day than controls for more frequent bowel movements (3.7 symptom-days compared with 2.8 symptom-days; difference, 0.9 symptom-days [CI, 0.1 to 1.8 symptom-days]; $P = 0.04$) (**Table 3**). In both groups, the median number of days on which olestra-labeled products were eaten was similar among participants who reported any gastrointestinal symptoms (20 eating days) and among those who reported no symptoms (21 eating days).

In almost all cases, symptoms were rated as having little to no effect on daily activities, and the groups did not differ in these ratings: 98.2% of the ratings in the olestra group and 97.2% of those in the control group indicated that symptoms either did not affect or only slightly affected daily activities (**Table 4**).

Because aggregate measures may obscure important differences in subgroups, we conducted a series of analyses to determine whether certain subgroups (children 2 to 12 years of age, teenagers 13 to 17 years of age, adults 18 to 64 years of age, elderly persons 65 to 89 years of age, and men and women) might be more likely to report effects of olestra (**Table 5**). When we stratified the groups by age, the groups did not differ significantly in the percentage of participants with gastrointestinal events for most gastrointestinal symptoms; the only exceptions were that more children in the control group reported other gastrointestinal symptoms (0.2% compared with 2.3%; difference, -2.1 percentage points [95% CI, -4.0 to -0.1 percentage points]; $P = 0.04$) and more adults in the olestra group reported gas (30.6% compared with 24.8%; difference, 5.8 percentage points [CI, 0.6 to 11.0 percentage points]; $P = 0.03$). Among children, the difference between

Table 2—Continued

Olestra Group			Control Group		
Average Amount of Chips Eaten Per Eating Day†			Average Amount of Chips Eaten Per Eating Day†		
Median	25th, 75th Percentile	90th Percentile	Median	25th, 75th Percentile	90th Percentile
←————— oz —————→					
1.30	1.01, 1.75	2.34	1.35	0.99, 1.90	2.67
1.41	1.05, 1.88	2.44	1.41	1.03, 1.98	2.79
1.24	0.97, 1.66	2.25	1.30	0.95, 1.83	2.55
1.13	0.88, 1.46	1.88	1.13	0.89, 1.54	2.18
1.37	1.00, 1.88	2.53	1.40	1.06, 1.82	2.55
1.39	1.07, 1.82	2.46	1.44	1.03, 1.99	2.87
1.38	1.07, 1.87	2.51	1.55	1.08, 2.14	2.96

the groups was mostly attributable to reported constipation. The only statistically significant difference between the test groups in terms of the number of symptom-days reported was that in the olestra group, the number of symptom-days was higher among adults for any gastrointestinal event (5.7 compared with 4.6 symptom-days; difference, 1.1 symptom-day [CI, 0.1 to 2.1 symptom-days]; $P = 0.03$) and more adults had more frequent bowel movements (4.1% compared with 2.9%; difference, 1.2 symptom-days [CI, 0.1 to 2.2 symptom-days]; $P = 0.02$).

When we stratified the test groups by sex, the percentage of men reporting nausea (3.9% compared with 7.4%; $P = 0.01$) and the mean number of symptom-days for cramping in men (1.8 compared with 2.5, $P = 0.04$) were significantly higher in the control group than the olestra group. Among women, the percentage of reported gastrointestinal symptoms did not differ significantly, but the numbers of symptom-days in the olestra group were greater for any gastrointestinal event (5.4 compared with 4.2 symptom-days; $P = 0.004$), gas (4.9 com-

pared with 3.7 symptom-days; $P = 0.009$), and more frequent bowel movements (3.9 compared with 2.9 symptom-days; $P = 0.03$). Although these differences in the numbers of symptom-days were statistically significant, they were small, consisting of only about 1 day out of a possible 42.

Of note, for all subgroups, the impact of symptoms on activities was minor; 98% to 99% of the ratings in the olestra group and 96% to 100% of those in the control group were in the “no effect” or “slight effect” categories (Table 4). In all subgroups except elderly persons, the impact of symptoms was slightly less in the olestra group than in the control group.

When participants were stratified by deciles of total olestra-labeled chips consumed, the percentage of participants in the highest decile who reported symptoms was greater in the olestra group than in the control group for more frequent bowel movements (27.9% compared with 11.7%; difference, 16.2 percentage points [CI, 5.0 to 27.4 percentage points]; $P = 0.005$) and looser stool (30.3% compared with 16.8%; difference, 13.5 percentage points

Table 3. Summary of Gastrointestinal Symptoms*

Event	Participants Who Reported GI Symptoms				Mean (\pm SE) Symptom-Days in Participants Reporting GI Symptoms			
	Olestra Group	Control Group	Difference (95% CI)	P Value	Olestra Group	Control Group	Difference (95% CI)	P Value
	<i>n</i> (%)		<i>percentage points</i>		←————— <i>symptom-days</i> —————→			
Any GI event†	619 (38.2)	576 (36.9)	1.3 (−3.6 to 6.2)	>0.2	5.0 \pm 0.3	4.2 \pm 0.3	0.8 (−0.1 to 1.6)	0.07
Heartburn	139 (8.6)	131 (8.4)	0.2 (−2.2 to 2.6)	>0.2	2.6 \pm 0.3	2.4 \pm 0.3	0.1 (−0.6 to 0.9)	>0.2
Nausea	93 (5.7)	131 (8.4)	−2.7 (−4.9 to 0.4)	0.02	1.9 \pm 0.2	1.7 \pm 0.1	0.2 (−0.3 to 0.8)	>0.2
Vomiting	29 (1.8)	28 (1.8)	0.0 (−1.1 to 1.0)	>0.2	1.3 \pm 0.1	1.2 \pm 0.1	0.1 (−0.3 to 0.5)	>0.2
Gas	392 (24.2)	339 (21.7)	2.5 (−1.8 to 6.7)	>0.2	4.5 \pm 0.3	3.8 \pm 0.3	0.7 (−0.2 to 1.6)	0.12
Bloating	182 (11.2)	146 (9.4)	1.8 (−0.8 to 4.6)	0.18	3.3 \pm 0.3	2.8 \pm 0.2	0.4 (−0.3 to 1.2)	>0.2
Cramping	243 (15.0)	236 (15.1)	−0.1 (−3.3 to 3.1)	>0.2	2.4 \pm 0.2	2.5 \pm 0.2	−0.1 (−0.6 to 0.4)	>0.2
More frequent bowel movements	332 (20.5)	271 (17.4)	3.1 (−0.7 to 7.0)	0.11	3.7 \pm 0.4	2.8 \pm 0.2	0.9 (0.1 to 1.8)	0.04
Looser stool	410 (25.3)	360 (23.1)	2.2 (−2.1 to 6.6)	>0.2	3.9 \pm 0.3	3.6 \pm 0.3	0.3 (−0.6 to 1.2)	>0.2
Other GI symptoms‡	36 (2.2)	50 (3.2)	−1.0 (−2.2 to 0.3)	0.12	2.3 \pm 0.4	2.1 \pm 0.4	0.3 (−0.8 to 1.3)	>0.2

* GI = gastrointestinal.

† Includes all participants who responded “yes” to the question in the daily record.

‡ The most frequently reported other GI symptoms in the olestra and control groups, by number of participants, were constipation (15 and 17), diarrhea (8 and 7), discolored stool (5 and 2), and hard stool (3 and 2). The remainder of other GI symptoms were reported by 3 or fewer participants.

Table 4. Effect of Symptoms on Daily Activities*

Category	Participant†	Noticed Symptoms but Daily Activities Were Not Affected	Noticed Symptoms and Daily Activities Were Slightly Affected	Missed Some Time from Daily Activities	Missed All Day
All participants					
Olestra group	619	2587 (83.6)	452 (14.6)	41 (1.3)	16 (0.5)
Control group	576	2021 (82.6)	357 (14.6)	46 (1.9)	22 (0.9)
Children (2–12 years of age)					
Olestra group	133	437 (87.9)	48 (9.7)	5 (1.0)	7 (1.4)
Control group	135	389 (81.0)	74 (15.4)	9 (1.9)	8 (1.7)
Teens (13–17 years of age)					
Olestra group	42	127 (84.1)	22 (14.6)	2 (1.3)	0 (0)
Control group	40	122 (86.5)	16 (11.4)	3 (2.1)	0 (0)
Adults (18–64 years of age)					
Olestra group	376	1741 (81.9)	346 (16.3)	29 (1.4)	9 (0.4)
Control group	342	1263 (81.0)	249 (16.0)	33 (2.1)	14 (0.9)
Elderly (65–89 years of age)					
Olestra group	68	282 (87.3)	36 (11.2)	5 (1.6)	0 (0)
Control group	59	247 (92.9)	18 (6.8)	1 (0.4)	0 (0)
Men					
Olestra group	252	944 (85.1)	149 (13.4)	11 (1.0)	6 (0.5)
Control group	238	854 (82.0)	163 (15.7)	19 (1.8)	5 (0.5)
Women					
Olestra group	367	1643 (82.7)	303 (15.3)	30 (1.5)	10 (0.5)
Control group	338	1167 (83.1)	194 (13.8)	27 (1.9)	17 (1.2)
High consumers‡					
Olestra group	53	331 (83.2)	58 (14.6)	6 (1.5)	3 (0.8)
Control group	63	269 (84.6)	44 (13.8)	4 (1.3)	1 (0.3)

* Participants rated the impact of their gastrointestinal symptoms on work, school, activities, or routine.

† Participants who reported any gastrointestinal symptoms.

‡ Participants in the highest decile for consumption of olestra-labeled chips.

[CI, 2.1 to 25.1 percentage points]; $P = 0.02$). The numbers of symptom-days did not differ significantly between the two groups for any of the eight symptoms, and symptoms were rated as having no effect or slight effect on 97.8% and 98.4% of symptom-days in the olestra and control groups, respectively (Table 4).

Seven participants in the olestra group and 9 in the control group reported visiting a physician for gastrointestinal symptoms. Medication use for gastrointestinal symptoms, reported by 132 participants in the olestra group and 129 in the control group, was also similar between the groups, including use of antidiarrheal agents (44 and 47 participants, respectively). No participant reported leakage of oil or fecal incontinence. One woman in the control group reported a gastrointestinal adverse event (cramping) that led to withdrawal from the study. Two controls died during the study; one committed suicide and the other had a fatal cardiac event.

At the end of the study, participants indicated which type of chips they thought they had been eating. More than half of the participants (58%) stated that they did not know which kind of chip they were eating. Of the 1283 participants who guessed at the type of chips they had been eating, 612 (39%) in the olestra group correctly believed that they had received olestra snacks and 175 (12%) in the control group correctly believed that they had received regular snacks. This difference in the per-

centage of participants who guessed correctly is consistent with the fact that a much higher proportion of the participants guessed that they were eating olestra snacks. Among participants who guessed, the percentage who believed that they were eating olestra chips (79%) was almost four times the percentage who believed that they were eating regular chips (21%).

Of interest, the percentage of participants reporting gastrointestinal symptoms was significantly higher among participants who thought they had been eating olestra chips (45.3% in the olestra group and 44.4% in the control group) than among participants who thought they had been eating regular snacks (31.0% in the olestra group and 29.1% in the control group) ($P = 0.01$). For participants who said that they did not know which type of chip they had been eating, the percentage reporting gastrointestinal symptoms did not differ between the olestra (35.0%) and control (35.8%) groups.

Discussion

In this large, controlled clinical trial in free-living adults and children, we found no difference in the occurrence of clinically significant or bothersome gastrointestinal effects between participants who consumed olestra or regular snacks for 6 weeks.

The amount of olestra consumed by the partici-

pants in this study was adequate to allow assessment of olestra's gastrointestinal effects. Approximately half of the participants ate olestra snacks on more than half of the 42 study days; this rate of consumption is considerably higher than typical chip consumption in the United States (11). On the basis of dietary survey data (12), 39% of the study participants would be classified in at least the 90th percentile for U.S. snack consumers; participants in the top decile for this study, therefore, had very high consumption. If participants had experienced unpleasant symptoms and had attributed them to chip consumption, one might expect that consumption would decrease over time. In fact, consumption was consistent throughout the study in both groups. Because olestra inhibits absorption of some vitamins and other nutrients, vitamins A, D, E, and K are added to offset this effect. Thus, we would expect to see no decrease in the serum levels of these vitamins, even in participants with very high chip consumption.

In general, the test groups did not differ in the occurrence of gastrointestinal symptoms, either overall or in the subgroup analyses. Even at the upper limits of the 95% CIs for the differences between the groups in symptom frequency and symptom-days, the risks over the 42-day study would not have been meaningfully greater in the olestra group. For example, for the participants in the highest decile for chip consumption, the upper confidence limit for the difference between groups in symptom frequency indicates that the percentage of participants with more frequent bowel movements could have been 27.4% greater in the olestra group. Even if this were the case, the difference would not be clinically meaningful because almost all of the symptoms reported had little or no effect on participants' daily activities (Table 4).

Although the mean number of symptom-days for any gastrointestinal event (women and adults), gas

(women), and more frequent bowel movements (all participants, women, and adults) was significantly greater in the olestra group, these differences were not clinically significant—only about 1 day out of a possible 42—and participants did not indicate that the symptoms were bothersome. Analysis of subgroups within the overall population indicated that these differences occur more frequently in adult women.

Previous clinical experience with olestra has also shown that increases in the frequency of bowel movements, if they occur, are minor and not clinically important. In a previous study, the frequency of bowel movements increased from 1.5 per day at baseline to 1.6 per day in participants who consumed 2.5 ounces of olestra chips per day and to 2.0 per day in participants who consumed 5 ounces of olestra chips per day (13).

In our study, the incidence of diarrhea and cramping was the same in the olestra group and the control group. The labeling on both the olestra-labeled packages and the informed consent forms told participants that they may notice cramping or loose stools. Despite the availability of this information, the occurrence of cramping was not greater in the olestra group than in the control group for the group as a whole or for any of the subgroups studied. In fact, the frequency of cramping was greater in the control group than in the olestra group among men. Of note, participants who ate the highest amounts of control (regular) chips reported loose stools and more frequent bowel movements less often than participants who consumed lower amounts of control chips.

Our results are consistent with those of other studies in which participants consumed olestra snacks under ordinary snacking conditions (5–8). The results of these randomized, controlled, double-blind trials do not substantiate anecdotal reports of severe diarrhea and abdominal pain or cramping

Table 5. Participants Who Reported One or More Gastrointestinal Symptom by Age and Sex*

Category	Participants Who Reported GI Symptoms				Mean Symptom-Days (\pm SE) in Participants Who Reported GI Symptoms			
	Olestra Group	Control Group	Difference (95% CI)†	P Value	Olestra Group	Control Group	Difference (95% CI)‡	P Value
	<i>n/n (%)§</i>		<i>percentage points</i>		<i>←—symptom-days—→</i>			
Age								
2–12 years	133/442 (30.1)	135/443 (30.5)	−0.4 (−8.4 to 7.6)	>0.2	3.7 \pm 0.4	3.6 \pm 0.4	0.2 (−0.9 to 1.2)	>0.2
13–17 years	42/125 (33.6)	40/102 (39.2)	−5.6 (−19.1 to 7.9)	>0.2	3.6 \pm 0.6	3.5 \pm 0.8	0.1 (−1.9 to 2.1)	>0.2
18–64 years	376/842 (44.7)	342/825 (41.5)	3.2 (−2.6 to 9.0)	>0.2	5.7 \pm 0.4	4.6 \pm 0.4	1.1 (0.1 to 2.1)	0.03
65–89 years	68/211 (32.2)	59/191 (30.9)	1.3 (−8.5 to 11.2)	>0.2	4.8 \pm 0.7	4.5 \pm 0.9	0.2 (−2.0 to 2.4)	>0.2
Sex								
Male	252/696 (36.2)	238/704 (33.8)	2.4 (−3.7 to 8.5)	>0.2	4.4 \pm 0.4	4.4 \pm 0.5	0.0 (−1.2 to 1.3)	>0.2
Female	367/924 (39.7)	338/857 (39.4)	0.3 (−5.3 to 5.9)	>0.2	5.4 \pm 0.3	4.2 \pm 0.3	1.3 (0.4 to 2.1)	<0.01

* Includes all participants who responded "yes" to the question in the daily record. GI = gastrointestinal.

† Values are the difference between the olestra and control groups in the percentage of participants who reported symptoms.

‡ Values are the difference between the olestra and control groups in the number of days on which participants reported symptoms.

§ Participants in the study group/participants who reported symptoms.

associated with olestra (4); instead, they show that under ordinary snacking conditions, gastrointestinal symptoms among participants who eat snacks containing olestra are no more troublesome than those associated with consumption of regular snacks containing triglycerides. This finding is of clinical importance: Physicians who see patients experiencing significant gastrointestinal symptoms that they attribute to olestra should seek other causes for these complaints, because our data indicate that these symptoms are unlikely to be related to olestra and may instead reflect a serious condition.

Our results did not indicate that the gastrointestinal symptoms following consumption of olestra were any more bothersome than those following consumption of regular chips. The only participants who withdrew from the study because of gastrointestinal adverse events were in the control group, and in the olestra group, 98% to 99% of ratings of effects on activities indicated that symptoms had no or slight impact on activities. In addition, the use of medications and physician visits for gastrointestinal symptoms were no greater in the olestra group than in the control group, and participants consumed olestra-labeled snacks at the same rate throughout the study regardless of whether they reported any gastrointestinal effects.

Several notable features of our study deserve comment. Through the use of daily diaries, we obtained detailed information on exposure (chip consumption) and outcomes (symptoms and functional impact). Special care was taken to blind study participants and staff to the study group assignments. Recruitment of participants from households known to be regular consumers of snack foods and provision of good-tasting products free of charge helped ensure that the dose of the study products would be adequate to allow determination of their effects on gastrointestinal symptoms and daily living. The study was designed to simulate real-world circumstances: Participants chose regular or olestra snacks from product displays, as they would in the marketplace, and consumed as much or as little as they wished while in their home environment.

The study was limited in that it relied on self-reports for information on chip consumption and gastrointestinal symptoms. However, there was no incentive to misreport this information and no reason to expect differential reporting between the olestra and the control groups. In addition, adults reported the information on consumption and symptoms for young children, the only practical means of collecting these data. The conclusions reached in this study were based on consumption of olestra in snack foods only. Olestra was not otherwise present in the participants' diets. Further studies would be required to determine the effects of

olestra consumed in foods in addition to savory snacks.

An interesting finding was the association of gastrointestinal symptoms with the type of chips that participants thought they were eating. Participants who believed that they were eating olestra chips reported gastrointestinal symptoms approximately 50% more often than participants who believed that they were eating regular chips, regardless of the type of chip they were actually eating. Among participants who said that they did not know which product they were eating, the percentage of participants reporting gastrointestinal symptoms was intermediate between the percentages of participants who guessed that they were eating olestra chips and those who guessed that they were eating regular chips. These findings suggest that reporting of symptoms may have been influenced by what the participants thought they were eating. They may also help explain anecdotal reports of gastrointestinal adverse events. According to a recent national survey (14), gastrointestinal symptoms are frequent in the population; up to 40% of adults report cramping, loose stools, or gas in the previous month. Marketed Olean packages state that olestra may cause abdominal cramping and loose stools. Consumers who have read this statement or heard reports of olestra-associated gastrointestinal effects may erroneously attribute these common symptoms to olestra.

In conclusion, our study demonstrates that clinically meaningful or bothersome gastrointestinal effects are not associated with unregulated consumption of olestra corn and potato chips in the home over 6 weeks.

From University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; and Procter & Gamble Co., Cincinnati, Ohio.

Note: Dr. Sandler is a consultant to Procter & Gamble Co. The terms of this arrangement are being managed by the University of North Carolina at Chapel Hill in accordance with its conflict of interest policies. Ms. Royer is an editorial consultant to Procter & Gamble.

Acknowledgments: The authors acknowledge Hill Top Research, Inc., Cincinnati, Ohio, for conducting the study.

Grant Support: By Procter & Gamble Co., Cincinnati, Ohio.

Requests for Reprints: Robert S. Sandler, MD, MPH, CB#7080, 326 Burnett-Womack Building, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-7080; e-mail, rsandler@med.unc.edu.

Current Author Addresses: Dr. Sandler: CB#7080, 326 Burnett-Womack Building, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-7080.

Drs. Zorich, Filloon, and Miday; Mr. Lietz; Mr. Brock; and Ms. Wiseman: Regulatory and Clinical Development, Food and Beverage Division, The Procter & Gamble Company, Winton Hill Technical Center, 6071 Center Hill Avenue, Cincinnati, OH 45224. Ms. Royer: 1 Deer Run Road, Ithaca, NY 14850.

References

1. **U.S. Food and Drug Administration.** Food additives permitted for direct addition to food for human consumption: olestra; final rule. Fed Regist. 1996; 61:3118-73.
2. **Mattson FH, Volpenhein RA.** Hydrolysis of fully esterified alcohols containing from one to eight hydroxyl groups by the lipolytic enzymes of rat pancreatic juice. J Lipid Res. 1972;13:325-8.
3. **Mattson FH, Nolen GA.** Absorbability by rats of compounds containing from one to eight ester groups. J Nutr. 1972;102:1171-5.
4. **Levine A.** Food fight in Indianapolis. U.S. News & World Report. 1997;May 5:53-4.
5. **Zorich NL, Biedermann D, Riccardi KA, Bishop LJ, Filloon TG.** Randomized, double-blind, placebo-controlled consumer rechallenge test of Olean salted snacks. Regul Toxicol Pharmacol. 1997;26:200-9.
6. **Koonsvitsky BP, Berry DA, Jones MB, Lin PY, Cooper DA, Jones DY, et al.** Olestra affects serum concentrations of α -tocopherol and carotenoids but not vitamin D or vitamin K status in free-living subjects. J Nutr. 1997;127(8 Suppl):1636S-45S.
7. **Zorich NL, Jones MB, Kesler JM, Carter SB, Sutton MA, Bayless T.** A randomized, double-blind study of the effect of olestra on disease activity in patients with quiescent inflammatory bowel disease. Am J Med. 1997;103: 389-99.
8. **Cheskin LJ, Miday R, Zorich N, Filloon T.** Gastrointestinal symptoms following consumption of olestra or regular triglyceride potato chips: a controlled comparison. JAMA. 1998;279:150-2.
9. **Lee EW.** Two-sample comparison for large groups of correlated binary responses. Stat Med. 1996;15:1187-97.
10. **Henderson WG, Moritz T, Goldman S, Copeland J, Soucek J, Zadina K, et al.** The statistical analysis of graft patency data in a clinical trial of antiplatelet agents following coronary artery bypass grafting. Controlled Clin Trials. 1988;9:189-205.
11. **Wuerthner J, Rickard A.** Consumer snacking behavior report. Snack World. 1992;Jan: SW1-SW35.
12. **Webb DR, Harrison GG, Lee MJ, Huang MH.** Estimated consumption and eating frequency of olestra from savory snacks using menu census data. J Nutr. 1997;127(8 Suppl):1547S-54S.
13. **Giannella R, Zorich N, Riccardi K, Filloon T, McRorie J.** Reports of diarrhea: when is stool water output clinically meaningful? A randomized controlled trial of olestra and sorbitol [Abstract]. Gastroenterology. 1998;114: A372.
14. **Sandler RS, Stewart WF, Liberman JN, Ricci JA, Zorich NL.** Digestive complaints in the United States—a national survey [Abstract]. Gastroenterology. 1998;114:A831.

Personae

In an effort to bring people to the pages of *Annals*, the editors invite readers to submit photographs of people for publication. We are looking for photographs that catch people in the context of their lives and that capture personality. *Annals* will publish photographs in black and white, and black-and-white submissions are preferred. We will also accept color submissions, but the decision to publish a photograph will be made after the image is converted to black and white. Slides or prints are acceptable. Print sizes should be standard (3" × 5", 4" × 6", 5" × 7", 8" × 10"). Photographers should send two copies of each photograph. We cannot return photographs, regardless of publication. We must receive written permission to publish the photograph from the subject (or subjects) of the photograph or the subject's guardian if he or she is a child. A cover letter assuring no prior publication of the photograph and providing permission from the photographer for *Annals* to publish the image must accompany all submissions. The letter must also contain the photographer's name, academic degrees, institutional affiliation, mailing address, and telephone and fax numbers.

We look forward to receiving your photographs.

Christine Laine, MD, MPH
Deputy Editor