Diet and Exercise and Gemfibrozil Therapy for the Management of Dyslipidemia:

A CEN* Study

W. Jack Stelmach, MD; David R. Rush, PharmD; Paul C. Brucker, MD; Ernst J. Schaefer, MD; Harmon E. Holverson, MD; William J. Kane, MD; and B. Leslie Huffman, Jr, MD

Kansas City, Missouri; Philadelphia, Pennsylvania; Boston, Massachusetts; Emmett, Idaho; and Toledo, Ohio

Background. Dyslipidemia constitutes a serious health problem that should be diagnosed and treated by the family physician. Little is known about the efficacy of typical dietary therapy for patients with abnormal cholesterol levels. This study was the first large prospective family practice evaluation of the effectiveness of diet-and-exercise therapy followed by a pharmacologic intervention for those patients who remained dyslipidemic.

Methods. Patients who met standard criteria for cardiovascular disease risk based on lipid analysis were enrolled in a typical 6-week physician-directed diet-and-exercise program. Those patients who were still dyslipidemic after that period were started on 12 weeks of pharmacologic treatment with gemfibrozil.

Results. Of the 2992 patients screened, 1193 were eligible for participation in the study. The diet-and-exercise program led to a modest change in lipid values (average decrease in total cholesterol of 4.1%). Only 2% of the patients achieved desirable levels of all lipid values. Seven hundred thirty-nine subjects qualified for further therapy and were treated with gemfibrozil. Seventy patients discontinued drug therapy because of adverse effects. Those who completed 12 weeks of pharmacologic therapy had an additional 5.4% reduction in total cholesterol, 3.9% reduction in low-density lipoprotein cholesterol, 30.6% reduction in triglycerides, and a 17.2% increase in high-density lipoprotein cholesterol.

Conclusions. These findings suggest that in a typical clinical setting, a nonpharmacologic intervention of diet and exercise may not produce the desired overall lipid changes in the majority of dyslipidemic patients.

Key words. Cholesterol; diet therapy; exercise; gemfibrozil. (*J Fam Pract 1993; 36:401-408*)

Nearly one half of the adults in the United States have total cholesterol levels above 200 mg/dL (5.2 mmol/L), which is associated with an increased risk of premature coronary heart disease (CHD).[1] In fact, dyslipidemias (low levels of high-density lipoprotein [HDL] cholesterol, high levels of low-density lipoprotein [LDL] cholesterol, high total cholesterol, or high triglycerides) constitute a serious health problem that should be diagnosed and treated by family physicians.

The National Cholesterol Education Program (NCEP) encourages physicians to increase their efforts to detect and treat such patients. Initially, nonpharmacologic interventions (eg, proper diet, exercise, and smoking cessation) are recommended. Diets that are rigidly controlled to decrease the intake of saturated fat and

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From the School of Medicine (W.J.S., D.R.R.) and School of Pharmacy (D.R.R.), University of Missouri, Kansas City; Thomas Jefferson University (P.C.B.) and Independent Blue Cross (W.J.K.), Philadelphia, Pennsylvania; Tufts University School of Medicine, Boston, Massachusetts (E.J.S.); Emmett Family Practice Center, Emmett, Idaho (H.E.H.); and the Department of Family Medicine, Medical College of Ohio, Toledo (B.L.H.). Requests for reprints should be addressed to W. Jack Stelmach, MD, Goppert Family Care Center, Baptist Medical Center, 6601 Rockhill Rd, Kansas City, MO 64131.

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cholesterol can reduce total cholesterol levels by an average of 10% to 20%.[2] To achieve these results, however, patients' compliance with these diets usually requires a great deal of encouragement and involvement by the physician and often additional professional help.

Many patients fail to achieve adequate reductions through recommended lifestyle modification, including diet, and require pharmacologic intervention. Yet, in a chart review survey of three family practices, Hudson et al[3] found that an intervention had been attempted with nearly one half of the patients with total cholesterol levels above 200 mg/dL (5.2 mmol/L), the most common intervention being diet (65 patients [73%]). Medication was used in only 8 patients (9%).

To date, there have been no studies to assess the effectiveness of pharmacologic interventions subsequent to a diet-and-exercise regimen in managing dyslipidemic patients in family practice.[3] A broad-based study was undertaken by the Clinical Experience Network (CEN) to assess the effects of diet and exercise alone, and in combination with drug intervention with gemfibrozil, on serum lipids in dyslipidemic persons in a heterogeneous family practice population.

Methods

Enrollment

A total of 2992 patients with a history of serum cholesterol levels ≥200 mg/dL (5.2 mmol/L) were screened by 327 CEN family physicians for inclusion in this prospective, open-label, multicenter trial. Informed consent was obtained from each patient. Physicians were recruited from the national roll of board-certified family physicians and were compensated for performance of physical examinations and the office visits. Laboratory services for their patients were provided free of charge. Medical and family histories were obtained from each patient to assess CHD risk factors as defined by NCEP guidelines.[4] A complete physical examination was performed, and fasting blood samples were obtained to determine total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol. Some of the patients who met entry criteria were assigned to a separate open-label, randomized trial of diet and exercise alone as opposed to diet, exercise, and gemfibrozil, which will be reported in a future publication.

Each physician was asked to enroll 10 patients of either sex who were over the age of 20 years and whose lipid profile met *all* of these inclusion criteria: total cholesterol ≥200 mg/dL (5.2 mmol/L); HDL cholesterol <40 mg/dL (1.05 mmol/L); LDL cholesterol 130 to 159 mg/dL (3.35 to 4.10 mmol/L) with CHD, or LDL cholesterol 160 to 189 mg/dL (4.15 to 4.90 mmol/L) with two or more CHD risk factors, or LDL cholesterol ≥190 mg/dL (4.90 mmol/L); and triglycerides <400 mg/dL (4.50 mmol/L).

Risk factors for CHD were male sex, a family history of premature CHD, cigarette smoking (>10 cigarettes/day), hypertension, diabetes mellitus, a history of definite cerebrovascular or occlusive peripheral vascular disease, and obesity (≥30% overweight). Exclusion criteria included pregnant or nursing women, patients with known contraindications to gemfibrozil, those who anticipated surgery or who had undergone surgery within the previous 6 months, and those who had taken probucol within the previous 6 months or any other lipid-lowering agent within the previous 6 weeks. Patients receiving concomitant therapy with steroid hormones or anticoagulants, or who had received an experimental drug within the previous 3 months also were excluded.

Treatment Plan

Patients meeting the inclusion criteria began a 6-week regimen that included a low-cholesterol, low-fat diet and an exercise program. A 6-week regimen was chosen because it is clinically practical in the family practice ambulatory environment; because the NCEP guidelines suggest an initial 4- to 6-week cholesterol check; and because previously published postmarketing efficacy and safety studies have used a 4-week restrictive diet.[5] Each patient received a copy of the American Heart Association diet book in conjunction with physician review of the material and recommendation of Step One or Step Two diet. The minimum exercise regimen consisted of a 30-minute walk three times a week; some patients exercised more vigorously.

A second lipid profile was obtained at the end of this 6-week period. If all lipid levels remained within inclusion ranges, the patient was eligible to receive gemfibrozil while continuing diet-and-exercise therapy; otherwise the patient was discontinued from the study. One 600-mg gemfibrozil tablet was administered twice daily, 30 minutes before the morning and evening meals, for 12 weeks if the following laboratory values were within normal limits: serum thyroxine, creatinine, alanine aminotransferase (ALT), and aspartate aminotransferase (AST).

An additional 179 patients already being managed with diet and exercise by their family physicians were enrolled at this stage of the study. These patients met all lipid profile enrollment criteria.

Schedule of Visits and Evaluations

Following initial screening, patients were scheduled for a visit after 6 weeks on the diet-and-exercise regimen, and after 6 and 12 weeks of diet and exercise in combination with gemfibrozil. At each visit, the patient's weight, blood pressure, and pulse rate were recorded. To assess compliance, the physicians were asked to rate how strictly the patient was following the diet-and-exercise regimen on a 5-point scale (1 = not at all, 2 = a little, 3 = somewhat, 4 = a lot, and 5 = very strictly). Patients taking gemfibrozil were rated for compliance on the same scale.

At each visit, blood samples were obtained for lipid determinations after a recommended 12-hour fast. All lipid analyses were performed by a central lipid reference laboratory certified by the Centers for Disease Control (MetPath Labs, Inc, Teterboro, NJ). The methods used for these lipid determinations were described in detail in a previous publication.[6]

Statistical Analysis

Statistical analysis was performed using SAS (SAS Institute, Cary, NC). Changes in lipid values and percent change of lipid values within subjects were tested for statistical significance using the paired *t* test and Wilcoxon matched-pairs/signed-ranks test. Statistical analyses of lipid values and percent change of lipid values between defined groups were performed using the unpaired *t* test and Wilcoxon rank-sum test. The selection of appropriate statistical methods and the use of transformation of the data were based on the properties of the observed distributions and assumptions underlying the various methods applied. When observed to be less than 5%, *P* values are reported herein; values greater than 5% are not viewed as being statistically important.

Means and standard errors (SE) were computed for each lipid value. Mean percent changes in lipid values at the end of the initial 6 weeks of diet and exercise were compared with initial values at study entry. The response of lipids to the addition of gemfibrozil was evaluated by comparing values at the end of 12 weeks of drug treatment with values obtained immediately before initiation of gemfibrozil therapy.

Results

Patient Flow

Screening produced 1371 patients who qualified, and 1192 of these entered the open-label diet-and-exercise program. The remaining 179 patients entered an open-label randomized trial and will not be discussed here.

Of the 1192 patients, 986 completed the study's diet-and-exercise phase and had their lipoprotein profiles reanalyzed. Patients not completing this phase (206) were lost to follow-up. Those whose lipid profiles still met the study criteria (n = 596) were eligible for continuation into the gemfibrozil phase of the study; 560 did continue. Three hundred ninety patients no longer qualified to continue in the study.

Also, at this stage, 179 patients who had completed some other diet-and-exercise program but were considered failures were allowed to join the study protocol because their lipoprotein profiles fit the criteria. With the inclusion of these patients, a total of 739 patients began drug therapy. Eventually, 641 patients completed the drug phase of the study, taking the drug for an average of 12 weeks (Figure).

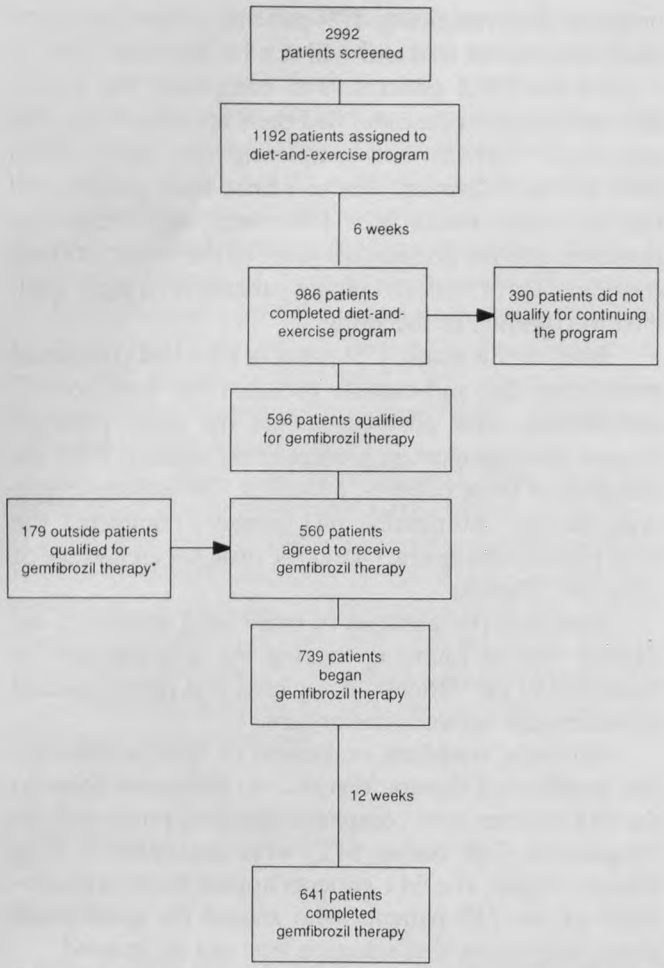
Statistical comparisons of entry lipid profiles of the patients lost to follow-up during the diet-and-exercise phase and of the 986 who completed that phase revealed no differences between the groups.

Similarly, statistical evaluation of lipid profiles before gemfibrozil therapy revealed no difference between the 641 patients who completed the drug phase and the 98 patients (739 minus 641) who discontinued drug therapy. Again, the 641 patients appear to be representative of the 739 patients who started the gemfibrozil phase, suggesting that selection bias can be ignored.

Demographic Data

Characteristics of the 2992 patients who were screened for study entry and their lipid profiles were described in a previous publication.[6] Typically, patients were white, overweight according to body mass index (BMI),[7] and in their mid-50s. A number of women failed to qualify for the study, principally because a low HDL cholesterol level was required for entry; nevertheless, women accounted for 29.6% (986) of the patients who completed the first phase of diet and exercise alone. The demographic profiles of those patients who completed the diet-and-exercise phase alone were similar to those for patients completing both phases (Table 1). The latter group, however, was slightly older.

In comparing nonlipid cardiovascular risk factors present in patients who entered the study before the diet-and-exercise phase (n = 1192) with those who entered before the drug phase (n = 179), the latter appeared to be at greater risk. This group had a higher incidence of all risk factors except for smoking (18.3% vs 24.7%). Among all patients, hypertension was the most



Flow chart showing sequence of 18-week program in the CEN study of the efficacy of diet-and-exercise therapy combined with pharmacologic intervention for dyslipidemia.
*Patients who were unsuccessful with previous diet-and-exercise therapy and met entry criteria for the study entered the pharmacologic treatment phase.

prevalent risk factor, followed by family history of CHD, smoking, and obesity.

Duration of Treatment

Six hundred forty-one patients took gemfibrozil for an average of 12 weeks (mean 80 days, range 32 to 128 days). Forty-four patients completed only 32 to 42 days of gemfibrozil therapy. Statistically, percent changes in the lipid levels of these patients were similar to those seen in patients who were taking the drug for a longer period, except for HDL cholesterol values.

Compliance with Prescribed Regimen

Assessments by physicians of compliance with the initial 6-week diet-and-exercise regimen and with subsequent treatment were similar. Compliance with diet and exercise during the initial 6 weeks, and when continued as subsequent therapy, was rated with a mean of 3.6 on a scale of 1 (indicating not at all) to 5 (indicating very strictly). Physicians rated compliance with drug therapy using the same criteria, resulting in a mean estimate of 4.5 on a scale of 1 to 5.

Table 1. Demographic Profile of the Dyslipidemic Patients

Characteristics	Patients Who Completed 6-Week Program of Diet and Exercise (SE) (n = 986*)	Patients Who Completed 12-Week Program of Diet, Exercise, and Gemfibrozil Therapy (SE) (n = 641*)
Age (y)	52.5 (0.41)	54.9 (0.51)
Weight (kg)	86.5 (0.52)	86.3 (0.66)
Height (cm)	173.2 (0.30)	173.0 (0.004)
BMI (kg/m^2)	28.8 (0.15)	28.8 (0.19)
Race		
White (%)	95.5	95.8
Black (%)	2.8	2.7
Other (%)	1.7	1.6
Sex		
Men (%)	70.4	71.3
Women (%)	29.6	28.7

**Complete data on certain patients not available.*
SE denotes standard error; BMI, body mass index.

Response to Diet and Exercise

At the end of the initial 6 weeks of diet and exercise, the 986 patients who completed that phase of therapy showed mean decreases, from initial values, of 4.1% in total cholesterol, 4.9% in LDL cholesterol, 0.2% in triglycerides, and 6.2% in the total cholesterol/HDL cholesterol ratio. Except for the triglycerides, these changes were statistically significant. HDL cholesterol values were increased by 5.5%, which was also a significant change (Table 2).

Table 2. Changes in Lipid Values After Diet and Exercise

Lipid	Lipid Values Before Diet and Exercise, mg/dL (n = 986)	Lipid Values After Diet and Exercise, mg/dL (n = 641)	% Change
Total cholesterol	261	250	−4.1*
Triglycerides	217	209	−0.20
HDL cholesterol	33	35	+5.5*
LDL cholesterol	192	182	−4.9*
TC/HDL ratio	8.08	7.51	−6.2*

**P < .001.*
HDL denotes high-density lipoprotein; LDL, low-density lipoprotein; TC/HDL, ratio of total cholesterol to high-density lipoprotein.

Table 3. Patients Who Were Nonqualifiers After Diet and Exercise

Lipid	Lipid Values Before Diet and Exercise, mg/dL (n = 390)	Lipid Values After Diet and Exercise, mg/dL (n = 390)	% Change
Total cholesterol	259	243	−6.1*
Triglycerides	222	220	+0.73
HDL cholesterol	34	38	+12.9*
LDL cholesterol	187	168	−9.6*
TC/HDL ratio	7.75	6.64	−13.6*

*P < .001.
HDL denotes high-density lipoprotein; LDL, low-density lipoprotein; TC/HDL, ratio of total cholesterol to high-density lipoprotein.

Table 4. Changes in Lipid Values After Diet, Exercise, and Gemfibrozil Therapy

Lipid	Lipid Values Before Treatment, mg/dL (n = 641*)	Lipid Values After Treatment, mg/dL (n = 641*)	% Change
Total cholesterol	254	239	−5.4†
Triglycerides	204	135	−30.6†
HDL cholesterol	32	38	+17.2†
LDL cholesterol	189	180	−3.9†
TC/HDL ratio	8.03	6.63	−16.4†

**Only 641 of the 739 patients initially recruited completed 12 weeks of therapy.*
†P < .001.
HDL denotes high-density lipoprotein; LDL, low-density lipoprotein; TC/HDL, ratio of total cholesterol to high-density lipoprotein.

Of the 986 patients completing the first phase of the study, 596 still had lipid profiles that qualified them for continued study; 390 patients no longer met all the qualification criteria. Comparing the lipid values of the nonqualifier group as a whole before and after diet-and-exercise therapy, there was a decrease in total cholesterol, LDL cholesterol, and total cholesterol/HDL cholesterol ratio (Table 3). The triglyceride values, however, remained virtually unchanged.

Thus, 11% (43) of the nonqualifier group were discontinued because their triglyceride levels had increased to ≥400 mg/dL; therefore, their LDL cholesterol levels could not be calculated. Eighty-nine percent (347) showed improvement in at least one lipid measurement beyond the limits set for the study continuance criteria. Only 2% (8) of these achieved "desirable" levels in all four lipid values, as described in the NCEP guidelines.[4] For the remaining 87%, the partial response to diet-and-exercise therapy, although disqualifying them from continuation of the study, did not necessarily reflect achieving an optimal therapeutic goal.

Response to Diet, Exercise, and Gemfibrozil

The cardiovascular risk-factor profile of those patients (n = 179) who entered the study just before the addition of gemfibrozil indicated a higher CHD risk profile than the other patients. Their mean lipid values at this stage, however, were similar to those noted in patients who continued in the study after the diet-and-exercise phase (n = 560). Changes after drug therapy also were similar.

Among all patients who completed drug therapy (n = 641), gemfibrozil was associated with additional mean decreases in total cholesterol (5.4%), triglycerides (30.6%), LDL cholesterol (3.9%), and in the total cholesterol to HDL cholesterol ratio (16.4%); HDL cholesterol additionally increased by a mean of 17.2%. All of these changes were statistically significant (Table 4).

A separate analysis of the percent changes in HDL cholesterol was also performed for the group of 44 patients who continued gemfibrozil therapy for only 32 to 42 days. Even though the measured change of 10.1% was less than the 17.2% observed over the average 12-week therapy period, it too was statistically significant ($P < .001$).

Safety

Safety was evaluated in the 739 patients who received at least one dose of gemfibrozil. One or more side effects considered to have been "probably" related to treatment were reported by 140 (19%) of the 739 patients. Seventy patients discontinued gemfibrozil because of reported adverse drug effects, accounting for 71% (70 of 98) of patient dropouts. The remaining 28 patients were lost to follow-up.

One hundred sixteen (57%) of the 205 total complaints were related to the gastrointestinal system or abdomen. Complaints included nausea (23 reports), dyspepsia (25), abdominal pain (16), diarrhea (15), constipation (9), flatulence (9), and eructation (8). Nongastrointestinal adverse events reported by more than 1% of subjects included headache and dizziness. There were six complaints of myalgia and one complaint of myasthenia. No new untoward or unusual side effects were reported.

Discussion

Our review of the literature indicates that this is the first prospective family practice evaluation of the effectiveness of nonpharmacologic and pharmacologic interventions in the management of dyslipidemic patients. Participants in the study were selected because of a history of elevated total cholesterol. Of the 2992 patients, 74% of the men and 41% of the women had low HDL cholesterol values (<40 mg/dL [1.05 mmol/L]) as well as elevated total cholesterol values (≥200 mg/dL [5.20 mmol/L]).[6] These high percentages were not unanticipated because the

population was preselected based on a history of total cholesterol levels ≥200 mg/dL (5.20 mmol/L) with other possible dyslipidemias. Demographic characteristics of the study population were representative of the average family practice.[8] The majority of patients were white men, and although both women and blacks were included, the percentage of each was comparatively small.

In this family practice patient population, diet and exercise alone had a moderate impact on dyslipidemia. Among the patients completing the initial 6 weeks, mean changes in lipid values from the time of study entry were modest. Total cholesterol, LDL cholesterol, triglycerides, and total cholesterol to HDL cholesterol ratio decreased 4.1%, 4.9%, 0.2%, and 6.2%, respectively; HDL cholesterol increased 5.5%. These changes reflect responses for the patients who qualified to continue into the drug phase of the study as well as for those who did not continue to qualify. The 390 nonqualifiers included patients whose responses were favorable in at least one lipid measurement: mean decreases in total cholesterol (6.1%), LDL cholesterol (9.6%), and total cholesterol to HDL cholesterol ratio (13.6%), and a mean increase in HDL cholesterol of 12.9%, and also patients (11%) whose triglycerides had increased to ≥400 mg/dL (4.52 mmol/L). Only eight patients (2%) achieved desirable levels in all lipid values.

The addition of gemfibrozil to the diet-and-exercise regimen of 641 nonrandomized patients subsequently induced additional statistically significant changes in lipid values. In particular, HDL cholesterol rose 17.2%, the total cholesterol/HDL cholesterol ratio decreased 16.4%, and triglycerides decreased 30.6%. Also, there were modest decreases in total cholesterol and LDL cholesterol (5.4% and 3.9%, respectively).

Some of the lipid changes observed could represent regression to the mean. However, most of this effect was observed during the first 6 weeks of diet and exercise; patients continuing in the study were less subject to this phenomenon.

These findings suggest that in a family practice setting, nonpharmacologic intervention with a regimen incorporating the recommendations provided in the American Heart Association diet book and general instructions for physical activity may not produce the desired overall lipid changes in the majority of dyslipidemic patients. This is not unexpected, as the NCEP notes that for optimum results, nonpharmacologic interventions should be employed in a "medical treatment setting" in which a team of professionals, including the physician, staff, and other specialists (eg, registered dietitians), closely monitors and repeatedly encourages the patient over an extended period (eg, 6 months).[4] In this setting, patients who rigidly control their consumption of saturated fat and cholesterol have been able to decrease total cholesterol by an average of 10% to 20%.[2] Many physicians, however, have neither the office personnel nor the outside resources to provide this level of support for their patients.

The limitations of nonpharmacologic interventions in controlling dyslipidemia in the family practice setting may require the physician to consider more rigorous dietary instruction or eventual pharmacologic intervention to achieve desirable results. This trial demonstrates that gemfibrozil is one pharmacologic intervention that can have a favorable impact on low HDL cholesterol, which is a major contributor to increased CHD risk.[9,10] In the heterogeneous patient population included in this study, gemfibrozil intervention was associated with mean increases in HDL cholesterol of 17.2% over values at the end of the initial 6 weeks of diet-and-exercise therapy. In addition, there were mean decreases in triglyceride levels after the initial phase of diet-and-exercise therapy of 30.6%. The total cholesterol to HDL cholesterol ratio decreased by 16.4%.

In conclusion, in a family practice office environment where rigid regimen controls are not practical, simple diet and exercise alone may achieve a modest degree of improvement in total cholesterol, LDL cholesterol, the total cholesterol to HDL cholesterol ratio, and HLD cholesterol in a heterogenous population with a wide geographic distribution. The addition of pharmacologic therapy with gemfibrozil to these same dyslipidemic patients can result in further significant changes in these values as well as in decreasing triglyceride levels.

It appears from the results of this trial that the family physician may need to implement more rigid nonpharmacologic therapy, with the addition of pharmacologic therapy when necessary, to achieve "desirable" goals in all lipid values.

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Clinical Experience Network

The following CEN investigators, listed in alphabetical order, participated in this study:

Abbott, Donald W., Yarmouth, ME; Acree, Martin V., Memphis, TN; Adams, Robert C., Van Wert, OH; Alexander, Bruce D., Easton, ME; Anderson, Leslie F., Lonoke, AR; Ausmus, Michael S., Kansas City, MO.

Baker, Charles E., Jr., Crossnore, NC; Barco, Daniel H., Durham, NC; Barger, Denver L., Little Rock, AR; Barmore, B.B. III, Thomson,

GA; Baughan, David M., San Diego, CA; Baxley, John B., Augusta, GA; Beamer, Thomas L., Santa Barbara, CA; Beaver, Steven R., Rensselaer, IN; Beaver, Walter P., Noblesville, IN; Beever, S. Chris, Dillon, MT; Bell, Gregory, Aurora, MO; Benski, Raymond, Nederland, TX; Benton, David E. II, Mesa, AZ; Bentz, Jerome W., Platte, SD; Bettis, Robert B., Edmonds, WA; Birkholtz, Karla L., Phoenix, AZ; Bjordahl, Kevin L., Webster, SD; Blaum, Gilbert E., Lincoln, IL; Bloom, Alan R., Webster, SD; Bodenhausen, Gary E., Blue Springs, MO; Borman, Richard J., Milwaukee, WI; Bosworth, Michael F., Dayton, OH; Bounds, Charles W., Moncks Corner, SC; Brody, Arnold G., St. Louis, MO; Brown, David M., Tacoma, WA; Brown, Michael J., Spearfish, SD; Brown, Sam F., Texarkana, AR; Brownstein, Bernard A., Philadelphia, PA; Broxterman, Steven J., Merriam, KS; Brubeck, Ellen T., Mt. Olive, NC; Bruner, Steven L., Lawrence, KS; Bryant, James W., Memphis, TN; Buchanan, Ralph W., Augusta, GA; Burnham, Jeffrey M., Baton Rouge, LA; Byler, Philip R., Williamsport, PA.

Cairns, Craig B., Granville, OH; Campbell, Jeanne M., Moncks Corner, SC; Campbell, Wayne L., Novato, CA; Carr, John P., Augusta, GA; Carrazzone, Peter L., Wayne, NJ; Carrico, Virgil N., Bryan, OH; Carter, Darrell L., Granite Falls, MN; Carter, John Z., Tucson, AZ; Castro, Miguel A., Jr., Towson, MD; Cavanaugh, Patrick R., Longmont, CO; Christensen, Ronald E., Anchorage, AK; Christiansen, Carroll D., Clarksburg, WV; Clutter, Robert E., Indianapolis, IN; Colodny, Charles S., Libertyville, IL; Cook, James A., Wheaton, IL; Cooper, Herbert P., Jr., Clemson, SC; Countryman, Phillip A., Indianapolis, IN; Cozine, Robert L., Emmetsburg, IA; Cripps, Hugh D., Smithville, TN; Cullison, Samuel W., Monroe, WA; Culpepper, Guy L., Dallas, TX.

Daniel, John M., Beckley, WV; Daniels, Timothy K., Storm Lake, IA; Darnell, John H., Jr., Ashland, KY; Dascoli, Thomas C., Indianapolis, IN; Daugherty, Joseph D., Jacksonville, AR; Davidson, Dennis O., Batesville, AR; Davis, Carl S., Lees Summit, MO; Davis, Larry E., Knoxville, TN; Davis, Robert W., Houma, LA; Davis, William B., Winters, CA; Dennis, Daniel P., Independence, MO; Dibble, F. Bert, Jr., Kingston, NH; Dieterich, Steven R., East Granby, CT; Dietrich, Peter S., Davis, CA; Dodge, Frederick A., Waianae, HI; Drain, Ray A., Edmond, OK; Dudley, Timothy E., Denver, CO; Dufresne, Duke, Schenectady, NY; Dunn, Luckey, Cabot, AR.

Emkes, Bernard J., Indianapolis, IN; England, Kent B., Hilton Head Isl, SC; Erb, Kent W., Sheridan, IN; Erickson, Daniel, Horicon, WI.

Fall, Gordon F., Seattle, WA; Feehan, John, Olathe, KS; Fields, Larry S., Ashland, KY; Fischer, Lee A., West Palm Beach, FL; Folse, Timothy E., Memphis, TN; Ford, John J. III, Westminster, CO; Frantz, Kurt S., Enid, OK; Frazzano, Arthur A., Portsmouth, RI; Frederick, Kenneth A., Cincinnati, OH; Freeland, Arthur G., Klamath Falls, OR; Frelinger, David P., El Segundo, CA.

Gardner, Henry J., Ogden, UT; Garver, Paddy R., Show Low, AZ; Gay, George L., Cambridge, WI; Gearhart, Judith G., Jackson, MS; Glenn, William B., Tuckerton, NJ; Glover, David W., Warrensburg, MO; Goldberg, Alan H., Pottstown, PA; Goldberg, Richard S., New York, NY; Gould, Randall K., Everett, WA; Greenlee, James R., Elkhart, IN; Greenstein, Seymour, Houston, TX; Gross, Thomas E., Mooresville, NC; Grossman, Ronald D., Hopewell, NJ; Gruca, Paul G., Riverdale, MI.

Hallinan, Timothy P., Gillette, WY; Hansen, Craig K., Rapid City, SD; Hanson, Mark T., Edmonds, WA; Harmon, Gerald E., Georgetown, SC; Harper, Diane, Kansas City, MO; Hartlage, Randall J., Tallahassee, FL; Hay, Robert F., Lawton, OK; Hayden, Timothy W., Jackson, TN; Hayes, Richard, Jacksonville, AR; Head, Gilbert, Omaha, NE; Heinemann, Daniel J., Canton, SD; Henderson, Audrey M., Augusta, GA; Hicks, David L., Little Rock, AR; Higgins, John M., Chico, CA; Himelstein, N. Harvey, Indianapolis, IN; Hitz, David L., Malvern, PA; Hochberg, Henry M., North Bend, WA; Hocutt, John, Jr., Wilmington, DE; Hoff, David L., Tallmadge, OH; Holsted, Carroll, King Fisher, OK; Hotz, Roy J., Jr., Kingsville, TX; Houston, Lawrence M., Overland Park, KS; Howard, Jerome, Charlotte, NC; Hromas, Richard L., Enid, OK; Hubbard, Daniel L., Englewood, CO; Huber, Joel, Redfield, SD; Huber, Thomas J., Pierre, SD; Hudson, C. Philip, San Antonio, TX; Hurst, Charles R., Tyler, TX.

Icaza, Ramiro, Jackson, MO; Ippel, Bruce D., New Castle, IN.

Jalowsky, Herbert R., Tucson, AZ; James, Gary V., Marion, KY; James, Trenton L. II, Baton Rouge, LA; Jamison, Kerstin C., Syracuse, NE; Jaworski, David A., Storrs, CT; Jeffries, Edward E., Baton Rouge, LA; Jones, David D., Presque Isle, ME; Jones, Michael A., Carson City, NV; Jones, Robert, Springville, UT; Jongewaard, Richard, Sioux Center, IA; Joseph, Ralph, Little Rock, AR.

Kahler, Mark R., Overland Park, KS; Kammerer, Donald J.F., Albert Lea, MN; Kaufman, Gary E., Yarmouth, ME; Kaufman, Harvey L., Voorhees, NJ; Keeler, George E. III, Washington, DC; Kelly, Carmel M., Pembroke, MA; Kelly, John J., Swannanoa, NC; Kendall, Thomas W., Greenville, SC; Kenny, John J., Manahawkin, NJ; King, Billy W., Millington, TN; Kipfer, Roger K., Louisville, CO; Kirkwood, Thomas S., Bicknell, IN; Kirsch, William A., Noblesville, IN; Kiteck, Stephen S., Somerset, KY; Knopp, J. Mark, Indianapolis, IN; Konzen, Dennis W., Mattawan, MI; Kowles, James A., Lebanon, NH; Kressenberg, Kenneth M., Novato, CA; Krier, David B., Carlton, OR.

Laker, Richard J., Fort Wayne, IN; Lam, Douglas E., Southern Pines, NC; Lammers, Keith A., Amherst, NH; Langston, Edward L., Indianapolis, IN; Lean, Edward W., Paw Paw, MI; Lee, Gerry M., Auburn, CA; Levalley, Gary L., Fort Dodge, IA; Levy, Mark R., Redmond, WA; Little, Robert G., Harrisburg, PA; Loewen, Nathan H., Hillsboro, KS; Loomis, Donald A., Tacoma, WA; Loschen, Darroll, York, NE; Lunceford, Travis E., Memphis, TN; Lushbough, Bruce C., Brookings, SD.

Mackey, Bruce A., Blackwell, OK; Maglothin, Douglas, Jonesboro, AR; Magruder, Thomas G., Omaha, NE; Maloney, Jay A., Thomson, GA; Mann, R. Jerry, Little Rock, AR; Martin, Joan B., Soda Springs, ID; Martin, Stephen, Yarmouth, ME; Martin, William G. III, Biddeford, ME; Mauk, Merlin H., Rancho Cordova, CA; Mauldin, Howard P., Oklahoma City, OK; Meisner, Carl R., Stafford, TX; Mgebroff, Arthur E., Yoakum, TX; Miller, Gary D., Orlando, FL; Miller, Ronald A., Whitefish, MT; Moore, Patrick F., Grand Forks, ND; Moquist, Dale C., Grand Forks, ND; Morris, Glenn F., Jackson, MS; Munger, Robert S., Jr., Exeter, NH; Myers, Carl M., Platt City, MO; McCullough, Dennis M., Lebanon, NH.

Nash, Bruce D., Bennington, VT; Neff, Robert, Humble, TX; Nelson, Darryl, Lees Summit, MO; Newbold, Stephen E., Kansas City, MO; Newman-Koehn, Mica, Marshall, MO; Nicewander, Robert K., Albuquerque, NM; Nicholson, B.E., Edgefield, SC; Novak, Dennis E., Forked River, NJ; Novak, Larry I., Syracuse, NY; Nunn, Roger E., Augusta, GA.

O'Shea, John M., Clinton, IA.

Page, William E., Palo Alto, CA; Paulding, Stephen B., Cumberland Ctr, ME; Pedigo, Thurman L., Sr., McMinnville, TN; Perry, Brian, Centre, AL; Petty, Russ, Devils Lake, ND; Phipps, Douglas R., Lander, WY; Pickell, Garfield, Hughson, CA; Pittard, Marion D., Toccoa, GA; Plessman, Paul E., Seward, NE; Pletzer, David P., Fishers, IN; Potter, Donald E., Canon City, CO; Preston, Bruce E., West Plains, MO; Purdy, Karen, Memphis, TN.

Raley, Steven P., Waco, TX; Randak, Adelaide L., Woodland Hills, CA; Rauholt, Dorthe, Augusta, GA; Reams, Calvin J., Thomasville, GA; Redka, James W., Williamsport, PA; Reimer, Jonathan E., Augusta, GA; Ridge, Fred R., Linton, IN; Rivell, William A., Martinez, GA; Robak, Lee M., Sauk City, WI; Roberts, Daniel D., Central Point, OR; Roberts, John H., Sioux City, IA; Roberts, Kenneth E., Dothan, AL; Rodgers, Charles H., Little Rock, AR; Rodrigue, Roger B., Wilmington, DE; Rogers, Jerry P., Moorhead, MN; Rose, Edward R., Carson City, NV; Roselli, Anthony M., Avon, CT; Rosen, Gary D., Seattle, WA; Rosen, Jeffrey B., Coral Gables, FL; Rothe, Thomas C., Tucson, AZ; Rothenberg, Robert A., Avon, CT; Rowland, Margaret, Yarmouth, ME; Rudberg, Theodore L., Scottsdale, AZ; Ruoff, Gary E., Kalamazoo, MI; Russell, Paul E., Spokane, WA; Rust, Richard E., Seattle, WA; Rutledge, Rion M., Rock Hill, SC.

Saffer, Jeffrey M., Cape Elizabeth, ME; Salanski, Stephen C., Lees

Summit, MO; Saloum, Herb A., Tyndall, SD; Saxer, John J., Leawood, KS; Saylor, Stephen, Topeka, KS; Scherger, Joseph E., Dixon, CA; Schlabach, Jay L., Goshen, IN; Schrader, Jane, Des Moines, IA; Schratz, Bruce, N. Little Rock, AR; Schroeder, Steve, Miller, SD; Scott, John G., Batesville, AR; Seeton, James F., Fort Collins, CO; Seklecki, Roger M., Augusta, GA; Shackelford, Robert H., Mt. Olive, NC; Sheppard, James M., El Dorado, AR; Sherrill, Leroy, Chattanooga, TN; Shives, Aaron, Watertown, SD; Simpson, Kirk W., Minneapolis, MN; Smith, Curtis, Camden, ME; Smith, Terry W., Chattanooga, TN; Smith, Thomas, Flora, IN; Snell, George F., Ogden, UT; Sockolov, Ronald, Sacramento, CA; Soll, Donald, Denison, IA; Spence, W. Dean, Bethany, OK; Spencer, Mark E., Arlington, WA; Stallings, Joseph H., Jr., Jonesboro, AR; Stanley, Richard E., Greeneville, TN; Stechschulte, Donald W., Jr., Pittsburgh, PA; Sternburg, Jon K., Narrowsburg, NY; Stout, Darrell L., Hooker, OK; Strassler, David M., Biddeford, ME; Stringer, Kenton L., Aurora, MO; Sullivan, James S., Dothan, AL; Swedberg, Jay A., Casper, WY; Sweiger, David W., Maple Valley, WA.

Tavani, Nicholas J., Jr., Laurel, MD; Terpstra, William G., Noblesville, IN; Thomas, Robert J., Ashland, KY; Tobin, Marla J., Higginsville, MO; Tocks, Jonathan B., Enola, PA; Towe, Benjamin F., Martinez, GA; Tremoulis, Edward L., Lima, OH; Turner, Kirby L., Poplar Bluff, MO; Turner, Richard B., Paradise, CA.

Van Gorp, David, Orange City, IA; Vicini, Henry T., Fall River, MA; Victor, Rafael D., Brooklyn, NY; Vinton, Thomas J., Liberty, MO; Virak, Roy H., Tacoma, WA.

Wanee, Neil R., Fishers, IN; Weber, James R., Jacksonville, AR; Weissberg, Robert A., Schenectady, NY; Welch, Michael C., Galway, NY; Wherry, Harry L., Longmont, CO; Wherry, Richard A., Dahlonega, GA; Wilhoit, Gordon B., Moncks Corner, SC; Wilkes, J. Thomas, Davis, CA; Williams, Henry W., Washington, DC; Williamson, Jay C., Akron, OH; Wingert, Kevin J., Clovis, CA; Winslow, James W., Tarboro, NC; Witters, Gregory D., Hermitage, TN; Woiwode, Daniel J., Edmond, OK; Wolf, Howard C., Lafayette, CO; Woodring, Mary A., Kingsport, TN; Wright, Keith A., Bolivar, MO.

Yaussy, Kenneth A., Newton, NC; Yeh, Tobias L., Ventura, CA; Yoder, Steven M., Goshen, IN.

Zebley, Joseph W., Towson, MD.

References

1. Consensus conference: lowering blood cholesterol to prevent heart disease. JAMA 1985; 253:2080–6.
2. Kris-Etherton PM, Krummel D, Russell ME, et al. National Cholesterol Education Program. The effect of diet on plasma lipids, lipoproteins, and coronary heart disease. J Am Diet Assoc 1988; 88:1373–1400.
3. Hudson JW, Keefe CW, Hogan AJ. Cholesterol measurement and treatment in community practices. J Fam Pract 1990; 31:139–44.
4. Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Arch Intern Med 1988; 148:36–69.
5. Bradford RH, Shear CL, Chremos AN, et al. Expanded Clinical Evaluation of Lovastatin (EXCEL) study results. I. Efficacy in modifying plasma lipoproteins and adverse event profile in 8245 patients with moderate hypercholesterolemia. Arch Intern Med 1991; 151:43–9.
6. Clinical Experience Network. Low high-density lipoprotein cholesterol and other coronary heart disease risk factors in patients with total cholesterol levels greater than 5.17 mmol/L (200 mg/dL) in family practice. J Am Board Fam Pract 1991; 4:285–97.
7. US Preventive Services Task Force. Guide to clinical preventive services. An assessment of 169 interventions. Baltimore: Williams & Wilkins, 1989:111–3.
8. Koch H, McLemore T. Highlights of osteopathic office practice, National Ambulatory Medical Care Survey, 1985. Advance data, vital and health statistics. No. 138. Hyattsville, Md: National Center for Health Statistics, 1987. DHHS publication No. (PHS) 87-1250.
9. Crouch MA. Assessing and managing hyperlipidemia. J Am Board Fam Pract 1988; 1:175–88.
10. Castelli WP, Garrison RJ, Wilson PWF, Abbott RD, Kalousdian S, Kannel WB. Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham study. JAMA 1986; 256: 2835–8.