What is the prognosis for acute low back pain?

EVIDENCE-BASED ANSWER The proportion of patients who are pain free or completely recovered after an acute episode of low back pain within 2 weeks to 6 months ranges from 21% to 90%, depending on the population studied and the method of measuring outcomes. The reported recurrence rates are also variable, from a low of 35% to a high of 75%, again depending on the length of follow-up and the study design. Grade of recommendation: C (on the basis of case-series, poor quality cohort studies, and case-control studies).

EVIDENCE SUMMARY It has been widely stated that 80% to 90% of attacks of acute low back pain resolve within approximately 6 weeks,[1] though there is little evidence to support this claim. Although there are many studies and guidelines regarding treatment methods for low back pain, few studies evaluate the natural history of low back pain. One prospective series in a primary care setting found that 90% of patients were without pain 2 weeks after initial evaluation by their physician.[2] This study had a 3-month follow-up period for 103 patients presenting with pain of less than 72 hours' duration.

Another prospective study found that 94% of patients evaluated for a new episode of low back pain were no longer visiting their physician for treatment after 3 months. However, this was not an adequate measure of resolution of pain. Only 21% (39/188) were pain free at 3 months and only 25% (42/170) were pain free at 12 months.[3] A larger study involved 1555 patients during a 6-month follow up after an episode of acute low back pain. The article reports a mean of 16 days to functional recovery, although only 69% of the patients considered themselves "completely recovered" at 6 months.[4]

Recurrences of low back pain are common. In one prospective cohort study of 443 patients with low back pain, 75% had a recurrence with a mean of 2 relapses in 1 year of follow-up, but only 228 patients completed the study.[5] Another prospective study of 208 patients found that 35% to 44% of patients had recurrence of pain within 6 months of their first episode, and 50% to 59% had a recurrence in 22 months of follow-up.[6] No studies identified findings or risk factors associated with higher recurrence rates.

RECOMMENDATIONS FROM OTHERS The Agency for Healthcare Research and Quality (www.ahcpr.gov) section on health outcomes (see http://www.ahcpr.gov/research/jan99/ra6.htm) states, "recent studies suggest that once experienced, low back pain becomes a part of life for almost half of those affected, and for many, it is intermittently disabling. Repeated visits and procedures do not appear to improve patients' long-term well-being, but they clearly account for substantial health care costs. Finally, back pain prognosis does not differ based on the type of provider initially seen or the level of practitioner confidence." This site offers several nice summaries of studies on low back pain.

Thomas E. Bielanski, MD
West Suburban Hospital Family Practice Residency
River Forest, Illinois

Joan Nashelsky, MLS
W.A. Foote Hospital
Jackson, Michigan

Read the clinical commentary by Anne Fitzsimmons, MD, at www.fpin.org.

REFERENCES

1. Dixon AJ. Rheumatol Rehabil 1973; 12:165-75.
2. Coste J, Delecoeuillerie G, Cohen de Lara A, Le Parc JM, Paolaggi JB. BMJ 1994; 308:577-80.
3. Croft PR, Macfarlane GJ, Papageorgiou AC, Thomas E, Silman AJ. BMJ 1998; 316:1356-9.
4. Carey TS, Garrett JM, Jackman A, et al. N Engl J Med 1995; 333:913.
5. van den Hoogen HJ, Koes BW, van Eijk JT, Bouter LM, Deville W. Ann Rheum Dis 1998; 57:13-9.
6. Carey TS, Garrett JM, Jackman A, Hadler N. Med Care 1999; 37:157-64.

What levels of cholesterol should be treated for primary prevention?

EVIDENCE-BASED ANSWER The levels of cholesterol that should be treated for primary prevention are based on low-density lipoprotein cholesterol (LDL-C) levels of > 100 mg/dL to > 190 mg/dL and vary according to whether the patient's risk is high, moderate, or low. See the table to estimate risk. Grade of recommendation for medication indications: A (on the basis of high-quality randomized controlled trials). Grade of recommendation for lifestyle indications: B (on the basis of extrapolations from randomized controlled trials).

EVIDENCE SUMMARY Statins are the most effective at reducing LDL-C and the associated cardiovascular risk. The 5-year West of Scotland study (WOSCOPS) showed that a 26% reduction in LDL-C (from a mean of 192 to 142 mg/dL) using pravastatin 40 mg per day reduced the risk of either nonfatal myocardial infarction (MI) or coronary heart disease (CHD) death (number needed to treat [NNT] = 42; relative risk [RR] = 31; 95% confidence interval [CI],17 - 43).[1] This trial enrolled middle-aged men with an LDL-C level > 155 mg/dL without a history of prior MI, although subjects with stable angina (5% of the participants) were still eligible. Similar reductions were seen in cardiovascular death and in all-cause death (RR = 22; 95% CI = 0 - 40). Lovastatin reduced the risk of a first major acute coronary event (NNT = 24) in the 5-year AFCAPS/TexCAPS trial that enrolled 5608 men and 997 women with below-average high-density lipoprotein cholesterol (HDL-C) (men, 36 mg/dL; women, 40 mg/dL) without signs or symptoms of CHD.[2] LDL-C was lowered 25% (from a mean of 156 to 115 mg/dL). Unpublished results suggest that simvastatin may have a similar effect. Primary prevention data are still lacking for atorvastatin and fluvastatin.

The 7-year Lipid Research Clinics Coronary Prevention Trial (LRC-CPPT) documented a reduction in CHD death and/or nonfatal MI (NNT = 59) with a 12.6% reduction in LDL-C with the use of cholestyramine, a bile acid resin, 24 g per day.[3]

Results of studies of the fibric acid derivatives are mixed. Subjects taking gemfibrozil 1200 mg per day in the 5-year Helsinki Heart Study had fewer coronary events compared with those taking a placebo (NNT = 71).[4] Subsequent analysis suggests that patients with a high LDL-C/HDL-C ratio (> 5) plus hypertriglyceridemia (≥ 205 mg/dL) benefited the most.[5] Clofibrate is no longer used because of an unexplained increase in deaths in the WHO Cooperative Trial.[6] To date, outcomes in fenofibrate trials have only focused on surrogate markers and not long-term clinical outcomes.

TABLE

Adult treatment recommendations from NCEP, Adult Treatment Panel III

Risk category	LDL-C level	LDL-C goal* at which to consider medication
Coronary heart disease risk equivalents	< 100 mg/dL	≥ 130 mg/dL; ≥ 100-129 mg/dL optional
2 or more major risk factors†	< 130 mg/dL	10-year risk‡ 10-20%: ≥ 130 mg/dL; 10-year risk‡ < 10%: ≥ 160 mg/dL
0 or 1 major risk factor†	< 160 mg/dL	≥ 190 mg/dL; 160-190 mg/dL optional

NOTE: CHD risk equivalents include symptomatic carotid artery disease, peripheral arterial disease, abdominal aortic aneurysm, diabetes, and a 10-year risk of > 20% (see ‡ below). The cut-off points for therapy for patients with clinical CHD are the same as for CHD risk equivalents.
* Initiate therapeutic lifestyle changes above these levels.
†Major risk factors include cigarette smoking, hypertension, HDL < 40 mg/dL, family history of premature CHD (CHD in first-degree male relative < 55 y; CHD in first-degree female relative < 65 y), age (men ≥ 45 y, women ≥ 55 y).
‡To calculate 10-year risk, use the Framingham Tables, available at http://www.nhlbi.nih.gov/guidelines/cholesterol/risk_tbl.htm.

RECOMMENDATIONS FROM OTHERS The recommendations of the Third Report of the National Cholesterol Education Program[7] (NCEP, Adult Treatment Panel III) are in the table. This report is an excellent source of additional information (http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf).

Terry L. Seaton, PharmD
St. Louis College of Pharmacy and Mercy Family Medicine

Susan Meadows, MLS
University of Missouri—Columbia

Read a clinical commentary by David Switzer, MD, at www.fpin.org.

REFERENCES

1. Shepard J, Cobbe SM, Ford I, et al. West of Scotland Coronary Prevention Study Group. N Engl J Med 1995; 333:1301-7.
2. Downs JR, Clearfield M, Weis S, et al. JAMA 1998; 279:1615-22.
3. The Lipid Research Clinics Coronary Primary Prevention Trial results. JAMA 1984; 251:351-64,365-74.
4. Frick MH, Elo O, Happa K, et al. N Engl J Med 1987; 317:1237-45.
5. Manninen V, Tenkanen L, Koskinen P, et al. Circulation 1992; 85:37-45.
6. WHO cooperative trial. Lancet 1984; 2:600-4.
7. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285:2486-97.

How beneficial are thiazolidinediones for diabetes mellitus?

EVIDENCE-BASED ANSWER The thiazolidinediones pioglitazone (Actos) and rosiglitazone (Avandia) are effective at lowering fasting plasma glucose (FPG) and glycosylated hemoglobin (Hb A_{1c}) in patients with type 2 diabetes when used either as monotherapy or in combination with sulfonylureas, metformin, or insulin. The glucose-lowering effects appear comparable with those of sulfonylureas and metformin alone. Currently, there are no randomized trials directly comparing patient-oriented outcomes of the thiazolidinediones with those of sulfonylureas and metformin. Grade of recommendation: B (on the basis of extrapolations from randomized trials and low quality randomized trials).

EVIDENCE SUMMARY Proper nutrition and exercise remain the cornerstones of diabetes therapy; medication management, however, is often necessary.[1] Both pioglitazone and rosiglitazone have similar glucose-lowering effects. See the tables in the online version of this Clinical Inquiry at www.fpin.org for a summary of monotherapy and combination clinical trials.

Pioglitazone has consistently been shown to decrease triglycerides and increase high-density lipoprotein and rosiglitazone increases total cholesterol, HDL, and low-density lipoprotein. The clinical significance of these effects has not been established. Both medications are generally well tolerated but have the potential to cause edema and mildly decrease hemoglobin and hematocrit.[2-9]

To date, there have been reports of pulmonary edema and hepatotoxicity associated with the use of rosiglitazone. In all cases, rosiglitazone was found to be a possible, not a definite, cause.[10-12]

RECOMMENDATIONS FROM OTHERS The American Diabetes Association and the American Association of Clinical Endocrinologists do not recommend one class of antidiabetic medication over another.[1,13] Both of the thiazolidinediones are indicated for monotherapy and in combination with a sulfonylurea and metformin. However, only pioglitazone is indicated in combination with insulin. They are highly metabolized by the liver and should not be used in patients with liver enzymes greater than 2.5 times the upper limit of normal. Routine liver monitoring is recommended at baseline, every 2 months for the first year, and then periodically thereafter.[1] Patients with New York Heart Association class III or IV heart failure should not use thiazolidinediones. In addition, thiazolidinediones cost considerably more than sulfonylureas and metformin.[14]

TABLE

Effects of rosiglitazone and pioglitazone, by dosage

Drug and dosage	Control	Adjunct medication	Change in Hb A_{1c} vs comparison (%)	Change in FPG vs comparison (mg/dL)
Rosiglitazone				
4 mg bid[2]	placebo	none	-1.5*	-73*
2 mg bid[3]	glyburide	none	+0.4	+5
4 mg bid			+0.2†	-11
8 mg bid[4]	placebo	metformin	-1.3*	-54.3*
2 mg bid[5]	placebo	sulfonylurea	-1.1*	-43.6*
4 mg bid[6]	placebo	insulin	-1.3‡	-55.8‡
Pioglitazone				
45 mg qd[7]	placebo	none	-1.6*	-65.3*
30 mg qd[8]	placebo	sulfonylurea	-1.3*	-57.9*
30 mg qd[9]	placebo	metformin	-0.83*	-37.7*

Hb A_{1c} denotes glycosylated hemoglobin; FPG, fasting plasma glucose; bid, twice a day; qd, every day.
*$P < .05$ versus control.
†P= not significant.
‡P= < .006 versus placebo plus insulin.
Find further details online at www.fpin.org.

Therefore, thiazolidinediones are not generally considered for first-line therapy.[15] These agents may be most beneficial in patients with insulin resistance and patients with renal dysfunction.[1]

Nicole S. Culbane, PharmD, BCPS
Wilkes University
Wilkes-Barre, Pennsylvania

Rebecca Graves, MLS
University of Missouri—Columbia

Read a clinical commentary by Steven Zweig, MD, at www.fpin.org

REFERENCES
1. The American Association of Clinical Endocrinologists. Endocrin Pract 2000;
2. Lebovitz HE, Dole JF, Patwardhan R, et al. J Clin Endocrinol Metab 2001; 86:280-8.
3. Charbonnel B, Lonnqvist F, Jones N, et al. Diabetes 1999; 48 (suppl 1):A114.
4. Fonseca V, Rosenstock J, Patwardhan R, et al. JAMA 2000; 283:1695-702.
5. Wolffenbuttel BH, Gomist R, Squatrito S, et al. Diabet Med 2000; 17:40-7.
6. Raskin P, Rendell M, Riddle MC, et al. Diabetes Care 2001; 24:1226-32.
7. Aronoff S, Rosenblatt S, Braithwaite S, et al. Diabetes Care 2000; 23:1605-11.
8. Kipnes MS, Krosnick A, Rendell MS, et al. Am J Med 2001; 111:10-7.
9. Einhorn D, Rendell M, Rosenzweig J, et al. Clin Ther 2000; 22:1395-409.
10. Thomas ML, Lloyd SJ. Ann Pharmacother 2001; 35:123-4.
11. Al-Salman J, Arjomand H, Kemp DG, et al. Ann Intern Med 2000; 132:121-4.
12. Forman LM, Simmons DA, Diamond RH. Ann Intern Med 2000; 132:118-20.
13. The American Diabetes Association. Diabetes 2001; (suppl 1):S1-S133.
14. Holmboe ES. Clinical applications. JAMA 2002; 287:373-6.
15. Inzucchi SE. Scientific review. JAMA 2002; 287:360-72.