- YOUR PAIN WAS REDUCED FROM 58 TO 43 ON THE SCALE.
- DOES THAT MEAN THAT I FEEL BETTER, DOC?
What are the types of medication benefits?

Most patients like you hope their medications will provide symptom relief, reduce the risk of complications from their medical condition, and/or improve their survival chances. Improvements in laboratory test measurements typically are not as important to patients, unless they reflect better control or prevention of their underlying condition. From the patient’s point of view, there are three main reasons to take a medication: to feel better, to reduce the risk of future disease complications, and to live longer.

What do we mean by feeling better?
Feeling better could mean having fewer or less severe symptoms, or it could mean (under ideal circumstances) the symptoms completely disappear. Symptom relief is the most common reason patients take medications. The list of common and typical symptoms is very long -- pain, itching, headache, nausea, dizziness, sleep disturbances, anxiety, depression, heartburn, constipation, fast heart beat, water retention, leg cramps, shortness of breath, and many more.

Feeling better also could mean improved quality of life, or what doctors call general or global well-being. It is possible to measure different factors of quality of life through rating scales that, for example, look at physical function or normal activities of daily living; the ability of the patient to interact with family, friends, and the community; the patient’s emotional well-being; overall life satisfaction; and perception of health. One advantage of measuring quality of life is that it helps identify those symptoms that are most bothersome and affect one’s daily life. This information, as well as communication with your doctor, can guide drug selection to improve your well-being.

Having one or more medical conditions does not necessarily mean you are suffering with bothersome symptoms or poor quality of life. Many conditions – like type-2 diabetes, for example – may cause few symptoms in the beginning. On the other hand, many elderly people with particular diseases or illnesses get used to their symptoms and are fairly satisfied with their overall health (for example, people with the milder forms of rheumatoid arthritis and osteoarthritis).

How do medications reduce the risk of future disease complications?
Mild to moderate increases in blood pressure seldom cause specific symptoms.
High blood pressure or hypertension often is first discovered during a routine blood pressure check in your doctor’s office. Most patients taking medication for their high blood pressure do not feel better when their pressure is controlled. But, in the long run, control of high blood pressure reduces your risk of developing major complications such as heart attack, stroke and heart failure. This risk is higher in those who also have other risk factors, such as smoking, diabetes and/or high cholesterol. Studies involving thousands of patients and lasting for several years have clearly shown that medications lowering blood pressure are very effective and especially reduce the risk of stroke.

**How can improved survival be determined?**
Most medical conditions do not shorten your life expectancy, although many serious conditions do. For these serious illnesses, improved survival rate is an important treatment goal. Proof of a survival benefit requires very large, long-term research studies. Some of these demonstrated improved survival, very likely due to specific medications prescribed to patients with various types of cancer and heart disease, type 1 diabetes, AIDS, and high blood pressure.

**How are treatment benefits measured and marketed?**
The alleviation of symptoms is the most common reason for seeking medical treatment. The desired effect is total symptomatic relief, which may or may not be achieved. Some patients have partial responses such as reduction in the severity and frequency of symptoms, while others get no benefit. The proportion with complete or partial responses can be measured and promoted as a percentage. For example, 70 percent -- or seven out of 10 patients -- may report a treatment benefit. It should be pointed out that some of this benefit is not a true medication effect (see Chapter 25).

The other major reason for medical treatment is to reduce the risk of future disease complications (events) to improve survival. This risk can vary a lot -- from less than 1 percent to much higher percentages -- for example, in patients with serious diseases in advanced stages. If six among 300 patients suffer an event during a year, the risk is 6/300. The risk of a complication or death is often expressed in the term “per 100 patient-years,” which in this case would be 2 events/100 patient-years.

In a clinical trial conducted to determine the benefits of a new medication, if the one-year complication rate is 24/1,000 in the comparison group and 16/1,000 in the actively treated drug group, the medication benefit is the difference: 8/1,000, or 0.8/100 patient-years. The inverse -- 1,000/8 equals 125 -- is referred to as the Number Needed to Treat (NNT). NNT equals the
number of patients that must be treated for one year in order to prevent one event. In considering the preventive effect of this medication, it should be noted that we have no way of knowing which patient of 125 will benefit, and that the 124 of 125 patients who receive no preventive benefit will be exposed to the adverse effects of the medication and may also have to bear its cost.

The morning headlines in your newspaper may one day report the results of a clinical trial that reads, “New drug reduces heart attack risk by 50 percent.” How should this report be interpreted, and is the reduction important? A reduction in the risk of a heart attack from 20 percent to 10 percent is a 50 percent relative reduction. This is an impressive number, but here is the problem: A reduction in heart attack risk from 1 percent to 0.5 percent is also a 50 percent relative reduction, but the change from 1 percent to 0.5 percent in absolute terms is not nearly as striking as the reducing the absolute risk from 20 percent to 10 percent. Newspapers and even some medical journals prefer to present the relative benefit because the size of the effect is more “impressive” and makes for more powerful news and headlines. We believe that promotion of the relative treatment effect can be very misleading. To you, the most important measure of event reduction is the absolute difference in the risk or the NNT. Be skeptical of headlines that report only the relative risk reduction; the difference in absolute risk is much more informative.

**What does surrogate benefit mean?**

Because of the effort, time, and high costs associated with performing a clinical trial that may demonstrate improved survival with a particular medication, not all medications undergo this type of testing. Attempts have been made to identify intermediate treatment effects that could be used as substitutes or “surrogates” for actual clinical benefits (for example, lowering blood pressure as a surrogate for reducing stroke risk, or decreasing cholesterol levels as a surrogate for reducing the risk of heart attack). The advantages of these surrogates are that the clinical studies can be smaller and take less time and money. The disadvantage is that a beneficial effect shown for a surrogate may not translate into an actual health benefit for the patient; for example, increased bone mineral density may not reduce bone fractures. More and more, scientists and government agencies are realizing the limitations of surrogates in testing new drugs. It is important to point out, however, that a large number of existing drugs were approved based on their effects on surrogate measures, including many drugs used for treating diabetes, irregular heart beats, high blood pressure and elevated cholesterol levels.

The fallacy of approving a new medication based on its effect on a
The most common drug benefits are relief of symptoms and improvement of quality of life.

Another type of benefit is preventing or delaying the onset of disease complications.

Medications may also improve survival.

Treatment benefits ought to be expressed in absolute, not relative, terms.

Surrogate measures of effectiveness often have limited clinical value.