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UNDERSTANDING RISK

Tricky Business

It happens all the time. You're reading a newspaper or watching the evening news and suddenly someone claims that apples are bad for you! You sit there bewildered because only yesterday you were sure that apples were one of the few things you could count on. You wonder how the so-called experts could be sure that apples are healthy one minute and so sure that they're dangerous the next. You can't figure out what's different, except that now a bunch of laboratory mice have been exposed to enormous quantities of pesticides and some developed cancer. Frustrated, you give up and decide to have a snack. In the refrigerator you bypass the fruit bin and grab a piece of pie.

Because we are mortal and because we live in an imperfect world, risk will always be with us. Consciously or not, as we go about our lives we weigh the relative risks and benefits of our actions all the time. Most often we act on imperfect and incomplete information. We do the best we can. Fortunately, even if we make the "wrong" decision it is likely to turn out to be all right. Something else, completely unexpected, will undoubtedly get us in the end. The world seen through nervous eyes is filled with peril: Is it safe to cross this street in the middle of the block? Dare I order french fries? Should I quit smoking even if that means I'll gain weight?

Commercial flight is one of very few areas where the degree of risk has been calculated and reduced about as far as is practical, and any further significant reductions would be prohibitively expensive. Once we walk off the airplane, however, our risks vary dramatically and are much more difficult to fathom, so we constantly make decisions based on more or less educated guesses.

Common sense

So how about them apples? Or, to put it a little differently, how can responsible individuals with no special expertise make intelligent decisions about all the information and misinformation that bombards us?

The same humble horse sense that keeps most of us from sticking our hand into the fire is an invaluable tool for sorting out what we read and hear. It's important to remember that news, by its very definition, is something new and unusual. No wonder that newspaper reports so often depart from what common sense tells us or what most experts believe. After all, the hundredth study showing a relationship between cholesterol and heart disease is hardly news, but the one study that fails to make such a connection is likely to become a headline. Clearly it would be silly for people to drastically change their lives on the basis of one newspaper article or a lone scientific study.

That doesn't mean we should throw out everything we read or hear. Once medical experts have reached consensus on a particular health issue, their message is amplified by the popular press and codified in guidelines issued by government agencies and national organizations. Today, for instance, there is widespread agreement that having a high blood cholesterol level is a risk factor for heart disease. And although new research confirming this relationship is strictly ho-hum for news editors, the health and science pages are filled with articles on how excess cholesterol should be managed. Even advertisements and labels on food products are broadcasting the cholesterol message.

Interpreting data

In spreading such established information, Harvard statistician and health policy expert Frederick Mosteller believes that the news media make an important contribution to public health. He points to the promotion of safe sex practices as a means for preventing the spread of AIDS as another example. This message has been repeated so often that now, said Dr. Mosteller, "the word condom is being used by very religious people and modest people in public discussion."

In most cases, however, less is known about what exactly constitutes a risk factor and how it can be reduced. How then can we interpret the health information that surrounds us? "The average consumer doesn't want to take a course in medical research," said clinical epidemiologist Thomas Chalmers, an adjunct professor of medicine at Tufts University School of Medicine and Dartmouth College. Still, there are some general principles that people can apply when trying to form intelligent opinions.

The first principle on Dr. Chalmers' list is that a particular finding should be the planned product of a study — rather than a casual observation — in order to mean anything. In other words, if a few people who use cellular phones got brain cancer, it does not necessarily follow that the phones were the cause of it. News reports about this kind of association can have a dangerous and disproportionate impact. Observed Dr. Chalmers, "There's a gradation from general anecdotal experiences, which are uncontrolled and subject to all sorts of bias, all the way to an exquisitely controlled randomized trial in which a specific question was asked and an answer obtained using appropriate scientific methodology."

But even in the best of studies, reanalyzing existing data can yield false results. In the first large trial that demonstrated the benefits of taking an aspirin during a heart attack, British scientists intentionally illustrated the limitations of a well-designed, controlled trial. In an analysis performed after the study was completed, researchers divided all the participants into groups according to their astrological sign. They found that Geminis and Libras did not appear to benefit from aspirin, which did help patients with other birth signs.

Of course, this does not mean that aspirin should be withheld from heart patients who are Gemini or Libra. The researchers published this finding with tongue in cheek, specifically to show the dangers of posing questions that a study was not designed to answer. By sheer play of chance, results for some subgroups will contradict the investigation's major findings. Unfortunately, these spurious results sometimes make sensational headlines.

Expert advice

One important safeguard against bad science is peer review, in which scientists scrutinize each other's work in advance. Almost all of the well-respected scientific journals rely on peer review to select papers for publication, and funding agencies use the process to determine which grant applications should be supported.

Any study that has not undergone peer review should be regarded with extreme skepticism. For example, one should be wary of findings announced at a press conference that do not accompany publication in a journal or a presentation at a scientific meeting.

At the same time, it's also true that peer review is no guarantee in and of itself that a study is good. For example, expert reviewers have no way of knowing if an investigator has falsified the data in an article. And even if a study is well-designed and scientifically valid, it may have absolutely no relevance to most people.

A less formal way of gauging the worth of a research report is to consider the opinions of experts who are quoted in the press, said cardiologist Lee Goldman, a professor of medicine at Harvard and chief medical officer at Boston's Brigham and Women's Hospital. "It helps a consumer to see what kinds of commentary a study evokes from people with expertise in the field. In other words, do some say, 'Well, it's all a bunch of hogwash,' or does there seem to be general support for whatever the finding is? That's not going to guarantee that something is accurate, but it may give us at least a little bit of consolation."

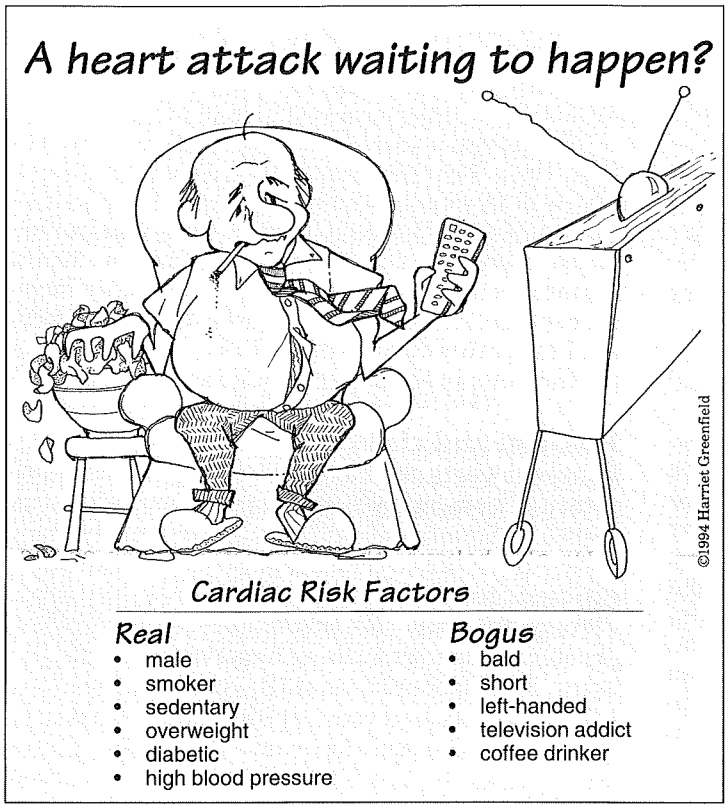
Our personal physicians are also important resources in matters like these, said Dr. Chalmers, although it is unrealistic to expect them to know everything or to have read every journal on the day it comes out.

He also believes that publications such as the *Harvard Health Letter* function as a tool for consumers, analyzing information and seeking expert perspectives in order to make sense of an issue. The American Heart Association, American Cancer Society, and other large voluntary associations are also reliable sources for information. These groups publish a wide variety of brochures and pamphlets for non-experts and issue recommendations about prevention and treatment.

Dr. Goldman points out that federal agencies such as the National Institutes of Health, the Occupational Safety and Health Administration, the Food and Drug Administration, and the Centers for Disease Control and Prevention also "help interpret the data and set reasonable guidelines." Although we may not think about it very often, most of us rely on the government to steer us away from a great many risky things.

Of mice and men

It is also important not to ask too much from a study, whether it is an *epidemiologic* or *experimental* one. In an epidemiologic investigation, scientists observe a sample group of people in order to determine the frequency and distribution of disease, or of good health, in a larger population. Because such a study is observational, it is a good way to uncover possible risk factors but it can never actually prove cause and effect. This is true simply because the interactions between humans and the environment are so complex that observation alone cannot prove that a specific attribute or behavior is to blame for development of a disease — especially a complex malady such as cardiovascular disease or dementia, for example. But a well-designed epidemiologic inquiry does eliminate many variables that could muddy the water and illuminates significant risk factors.



One reason that epidemiologic results alone shouldn't be used to set public health policy or determine how a disease should be treated is that it is easy to confuse an apparent risk factor with a real one. Some studies show that baldness, for example, appears to be associated with an increased likelihood for developing coronary disease. But we can be pretty sure that baldness itself doesn't lead to heart attacks. Instead, baldness may be a marker for something that does harm the heart — such as too much or too little of a hormone or circulating chemical — rather than a risk factor *per se*. It would obviously be absurd to try to prevent heart disease by treating baldness.

In contrast to epidemiologic studies, which scrutinize the complexity of real life, experiments are a systematic way of testing the effects of one particular variable, such as a risk factor or a drug, under tightly controlled circumstances. For example, a group of identical mice living in sterile quarters can be randomized into two groups and given either an active pill or a placebo. Any differences that emerge between the groups should be attributable to the variable — in this case the pill — that was manipulated. But treatments that work in animals should never be applied directly to humans for several reasons.

For starters, of course, people are not lab animals. Mice and other small creatures aren't naturally subject to many of the common ailments that afflict humans, so scientists have to alter them genetically or physiologically to create animal "models" for human diseases. These are interesting and useful to scientists, and often pave the way for important advances, but they don't tell doctors which medicines to prescribe.

Clinical trials, which are experiments performed on people, have their own limitations. Although the results of such studies can be extremely valuable, savvy consumers always ask certain questions.

Were the treatment and control groups adequately *randomized*? Randomization is one of the chief methods by which scientists fight *bias* (the distortion of findings by irrelevant factors). However, it is always possible that two randomly selected groups will differ in ways that skew the results, especially when the number of participants is not very large.

Was the trial *double-blinded*? In other words, were both investigators and participants ignorant of who received active treatment and who received an inactive placebo? The brain is a powerful organ indeed, and both investigators and participants may see and feel what they expect to see and feel. Time after time scientists have observed a powerful placebo effect in people who believe they are taking active treatment. However, it is not always necessary or desirable to compare an active treatment with a placebo. For example, new medicines or operations are often compared with the best existing therapies.

Was this a *multicenter* trial or was it performed at one institution only? If a study is done at one hospital, it is always possible that its equipment, procedures, or the expertise of its staff are unique and can't be duplicated elsewhere. Thus a multicenter trial is nearly always preferable to a single-center study. For example, the conclusions of a multicenter study can still be valid, even if one center supplied fraudulent data.

Reaching a conclusion

Let's imagine for a moment that we've read a report about a new clinical trial and all the signs look pretty good: its results confirm those from similar trials and the experts seem to agree that it was well designed and generated valid information. Now comes the hard part: how can each of us integrate the new findings into our own lives?

One point to keep in mind while grappling with this question is the simple fact that each of us dies only once, so that most risk factors will end up as bystanders instead of actors in the final drama. A person who has advanced lung cancer, for example, can stop worrying about cholesterol. As for every-

one else, "if you have a family history of heart disease, if you smoke, or especially if you've already had a heart attack, then you should be very concerned about cholesterol," said Dr. Chalmers.

It also helps to remember that risk factors do not exist in isolation. Imagine for a moment that apples, or at least something people spray on apples, may in fact increase the risk for cancer or some other disease. If we react to this finding by substituting a pear or an orange for an apple, we may have marginally improved our risk-factor profile. But if we eliminate apples and replace them with french fries, we've almost certainly worsened our profile — in more ways than one!

Sometimes this broader perspective on risk factors gets lost in the breathless shuffle to deliver the news. Consider how stories about breast cancer in women have been reported in recent years. Many women have rejected the use of estrogen, which may reduce the incidence of heart disease and osteoporosis, because they fear that it might increase the likelihood for developing breast cancer. However, only 2.8% of Caucasian women between the ages of 50 and 94 die from breast cancer, compared with 31% who die from heart disease. Even a back-of-the-envelope calculation indicates that, for most women, the beneficial cardiovascular effects of estrogen replacement far outweigh its risks as a breast cancer promoter. Unfortunately, this perspective is seldom emphasized in the popular press, and when it is, it rarely gets the headlines.

Lies and statistics

Benjamin Disraeli said that there are three kinds of lies: lies, damned lies, and statistics. It is possible to prove statistically that the average U.S. citizen has one testicle, for instance. The point is that statistical methods are tools and that they can produce blatantly wrong conclusions unless sensibly used.

When scientists report their findings, they speak of certain results as *statistically significant* — a term that means little to most people. As it happens, scientists have arbitrarily agreed that the results of a study are not considered statistically significant unless the probability that its results are due to chance alone is less than one in twenty. Because thousands of clinical trials are performed, however, some studies that yield statistically significant results eventually turn out to be wrong.

Even valid results may be less relevant to our own lives than we think at first. Most of us would be impressed if told that risk factor A increases our risk of disease X by 100%. And we would probably be less impressed if we were told that risk factor B increases our risk of disease Y by 25%. But if the baseline risk for disease X is only 1 in 1,000, factor A would raise it to only 2 in 1,000. On the other hand, if the baseline risk for disease Y is 400 in 1,000, then factor B would increase our risk for disease Y by 100 cases, to 500 in 1,000.

The increase in *relative risk* is greater in the first case, but the increase in *absolute risk* — which is what really matters — is greater in the second. It's good to be skeptical of claims that a risk factor increases the likelihood of cancer, heart disease, or anything else by an improbably large percentage. Ask some basic questions: How likely am I to get this disease in the first place? Were the participants in the study at all similar to me?

Realism and risks

In recent years we have all become increasingly aware of how our personal habits may affect the length and quality of our lives. In a relatively short time there have been dramatic changes in attitudes toward drinking and driving, smoking, dietary fat, and the importance of controlling chronic conditions such as hypertension and diabetes. Even before these shifts occurred, however, life expectancy had been rapidly rising as a consequence of better sanitation and the advent of vaccines and antibiotics. The impact of these advances has been so great that they may never be matched, even if cigarettes and cheeseburgers disappeared from the planet.

If heart disease, the nation's number one killer, could be completely eliminated, the average American's life span would increase by only three years, according to an analysis conducted by Harvard's Dr. Goldman and his colleagues. Because so many of us already live well into our 70s, we may have little to gain from altering our behavior in ways that diminish our enjoyment of life.

On average, a 35-year-old man will add one year to his life expectancy by lowering his diastolic blood pressure to 88 mmHg, eight months by lowering his cholesterol to less than 200 mg/dl, and 10 months by quitting smoking. If, however, bringing risk factors under control heads off a premature heart attack in the 40s or 50s, the gain for that individual is substantial.

Because perspective is so often missing from reports about risk factors, some people focus on the latest details at the expense of the big picture. After all, it's silly to worry about having missed one's daily beta carotene supplement while smoking the twentieth cigarette of the day.

Other people pursue a healthy lifestyle so doggedly that it becomes a full-time job, supplanting the activities that once added zest and meaning to daily life. When this happens, perhaps it helps to remember that in life, quality is every bit as important as quantity.

— LARRY HUSTEN, Ph.D.