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Trusted advice for a healthier life

The top 10 health stories of 2009

As we were putting together this year's top 10 list, uncertainty became a motif. Here at the beginning of the flu season, we don't really know if the H1N1 flu pandemic will stay controlled by public health measures, or take off in some unexpected way. Will the yearlong debate over health care reform result in something significant — or wind up being political sound and fury, signifying stalemate?

Even when a large randomized clinical trial seems to have settled an important matter, it's hard to say how the findings will be applied exactly. Results from a large study of intensive care unit patients showed that controlling blood sugar levels too tightly was a bad idea (number 7 on our list). But finding the right level of control — that's a work in progress. The JUPITER study may usher in a new era of cardiovascular disease prevention that emphasizes inflammation and lowering C-reactive protein (number 8). But how will those goals be combined with tried-and-true cholesterol control? Also a work in progress.

More black-and-white answers would be nice, but learning to live with gray areas is, perhaps, the beginning of wisdom, and not just in health and medicine.

1. No panic about this pandemic

After the first several weeks of uncertainty, most of the news about the 2009 H1N1 "swine flu" pandemic has been reassuring. Much of that has to do with the nature of the H1N1 virus itself, which spreads easily and makes people sick, but so far rarely in a life-threatening way. And the word pandemic is misunderstood: a disease is considered pandemic if it has spread globally and affects a larger-than-usual proportion of the population. The disease needn't be severe. But a major reason for the calm has been the measured public health response. Plenty of information has been made available (this is the first Internet-age pandemic). A vaccine was developed and put into production, although shortages are a serious concern. Health officials gave us simple, concrete things to do to protect ourselves and others: cough and sneeze into your sleeve, wash your hands often, get vaccinated with both the seasonal and H1N1 flu vaccines, stay home if you're feeling sick.

This wasn't the flu pandemic that the experts were expecting. For years, they've eyed the H5N1 bird flu virus circulating in Asia to see if it would mutate and become transmissible among humans. Instead, H1N1 emerged in Mexico with a complicated quadruple pedigree: two strains of swine flu, a human strain, and a bird one. Hospitalization and death rates from the new virus have been high in healthy young adults and quite low in people older than 60. One explanation for that pattern is that older people may have some immunity left over from exposure to a previous version of H1N1.

We have months of flu season ahead of us. Much could go wrong. Flu viruses are more contagious and more likely to produce severe illness in cold, dry air. They can mutate. Still, early indications were that this pandemic will stay manageable. As expected, flu rates in the Southern Hemisphere returned to normal in the fall. When we went to press, the worldwide death toll was

about 5,000 — a modest number, all things considered. And most Americans were going about their business, with cleaner hands than ever before.

2. Health care reform: Half a loaf

The final version was still taking shape as we went to press, but some basic elements of health care reform looked to be in place. A mandate requiring individuals to buy health insurance seemed likely. We may also see tighter regulation of the health insurers (no turning away people for pre-existing conditions) and creation of computerized "exchanges" where people and small employers can shop for affordable policies. About 46 million Americans lack health insurance, and these and other reforms should shrink that number. By how much depends on details like the subsidy levels for those who can't afford insurance and whether a new government insurance program, the so-called public option, comes to be.

Expanding coverage will be no small feat, but it's a breeze, politically, compared with reining in spending. Chances are that 2009's reforms won't do enough on the cost side, and there's no consensus on how to proceed. Technology (new drugs, new tests) has been the driving force behind health care spending for decades. Some economists see technology's effects as easing up and that it could even save money in the future. Let's hope they're right.

3. Bad fat, good fat

In real estate, it's location, location, location. The same may be true for body fat — and color makes a big difference, too.

The visceral fat — the fat located in our abdomen — churns out inflammatory factors and hormones. By comparison, the subcutaneous fat, which lies under the skin, is metabolically sedate. Findings published in 2009 further implicate visceral fat as a source of health woe, while largely exonerating the subcutaneous deposits. For example, Framingham Heart Study researchers reported that visceral, not subcutaneous, fat was associated with calcium deposits, a marker for atherosclerosis, in the body's main artery, the aorta.

White fat cells store fat, and most of the fat in our bodies — visceral and subcutaneous — is white fat. But there are also brown fat cells that actually burn fat. We have brown fat as newborns to help with the regulation of body heat, but it's long been believed that it soon disappears. A surprising trio of articles published in *The New England Journal of Medicine* used PET scans to show that we actually retain appreciable amounts of brown fat as adults in an area between the shoulder blades, and that the more brown fat an adult has, the more likely he or she is to be lean with healthy metabolic indicators.

Researchers are now studying how brown fat cells can be increased or activated. The visceral fat findings are shifting attention to waist size as a measure of obesity, although it's not so simple: subcutaneous fat also contributes to waist size, especially in women. Still, the notion that diet and other habits should be judged by their effect on waist circumference is gaining traction.

4. Curbing the doctor-industry relationship

Companies — particularly drug manufacturers — spend billions each year promoting their wares to doctors. In 2009, a wave of new rules and regulations went into effect to slow down the flow of gifts (all those logo-embazoned pads and pens), free meals, and payments to physicians. The changes were made in response to criticism that industry largesse was creating conflicts of interest. Too often, there was a risk that the doctor-industry relationship would taint the doctor-patient one.

Large teaching hospitals, including the Harvard-affiliated Partners HealthCare system, barred their faculty from accepting gifts and meals and participating in speaker bureaus. Industry groups and professional societies revised their codes of conduct. Massachusetts and several other states stepped in with gift bans and disclosure requirements. And there is a good possibility that the health care reform legislation will include a requirement that drug and device makers report their payments to doctors on a public Web site.

Industry funding is important in medicine, especially when it comes to research. But it should be aboveboard, for all who are interested to see. The moves toward full disclosure and the end of cheesy gifts designed to curry favor are steps in the right direction.

5. At last, maybe an alternative to warfarin

Millions of people depend on warfarin (Coumadin), especially those with atrial fibrillation, a common heart rhythm disorder. By blocking vitamin K, the drug reduces the risk for blood clots and, in turn, for stroke and other life-threatening, clot-related disorders. But warfarin interacts with dozens of drugs, herbs, and foods. Frequent blood tests are often necessary to make sure the blood's clotting capacity is in a safe range. Patients and their doctors have accepted these drawbacks for lack of a good alternative. But in 2009, one might have been found.

Dabigatran, which is already approved in Europe for limited purposes, acts directly on thrombin, one of the key players in the formation of blood clots. No blood monitoring is needed, and because of the way the drug is metabolized, there are far fewer interactions to worry about. A large, industry-sponsored study (18,000 atrial fibrillation patients in 44 countries) was organized several years ago to test two different doses of dabigatran (110 mg and 150 mg) against warfarin. The results show that dabigatran matches up well against warfarin. At the smaller dose, it was just as effective at preventing strokes and caused fewer major bleeds. At the larger dose, it was more effective than warfarin at stroke prevention and caused a similar number of bleeds. The news wasn't all good: heart attacks and gastrointestinal side effects were more common among those taking dabigatran than those taking warfarin.

The FDA is expected to approve dabigatran in 2010. It will undoubtedly be more expensive than warfarin, although blood tests won't be needed, so that might help offset some of the additional expense. People who don't need frequent blood tests and dose adjustments may be better off sticking with the old standby, warfarin, but the convenience and efficacy of dabigatran is likely to be a real advantage for many patients.

6. These micros are major

Messenger RNA reads the DNA of our genes and uses that code to assemble proteins, the building blocks of all forms of life. In the mid-1990s, researchers discovered small bits of RNA, now known as microRNA, that attach to the messenger version and switch it off, so the protein doesn't get made.

Already microRNAs are playing an important role in helping cancer doctors make more accurate diagnoses and prognoses and choose more effective treatments. For example, in 2009, researchers reported that liver cancer patients whose tumors had lower levels of a particular microRNA, called miR-26, had a much worse prognosis, but also a better response to one kind of treatment.

Promising results for macular degeneration and respiratory syncytial virus infection have been reported in humans, and successful treatments using microRNAs have been achieved in mice. Results of a mouse study showed that delivering miR-26 to liver cancer cells made them behave more like normal cells. Another study in mice showed that delivering a different microRNA to breast cancer cells prevented them from metastasizing.

Compared to drugs, microRNAs are easy and cheap to manufacture. For cancer, they would mean treatment targeted at the root cause of the disease: mutated genes promulgating wayward proteins. And researchers have high hopes that microRNA medicine will yield pinpoint control, so only diseased cells would be affected. But there's also reason to mix in some caution with the optimism. MicroRNA research is, after all, in the beginning stages and has a good ways to go before maturing into full clinical reality. Toxicity could be a big hurdle if therapeutic microRNA accidentally interferes with messenger RNA that shouldn't be interfered with.

7. Blood sugar levels: Seeking the sweet spot

High blood sugar levels aren't just a problem for people with diabetes. Elevated blood sugar is associated with worse outcomes for heart attack and stroke patients and, in fact, for hospital patients of all kinds. Several years ago, Belgian researchers published results showing that the sickest of the sick — patients in intensive care units (ICUs) — fared far better if their blood sugar levels were very tightly controlled. That study was influential, partly because it fit so nicely with the conventional wisdom about the perils of sugary blood. Guidelines were revised, so tight blood sugar control, accomplished with intravenous infusions of insulin, became a priority in ICUs throughout the country.

Now it's looking like those guidelines may need to be revised again. Results from a large randomized trial (too cutely called the NICE-SUGAR trial) showed that the death rate for tightly controlled patients was *higher* than it was for patients controlled to more conventional levels. The difference was 2.6 percentage points (27.5% vs. 24.9%), which may not seem like much but translates into many deaths given the number of ICU patients.

Doubts about the wisdom of aggressive blood sugar levels aren't limited to the ICU. Study results featured in our top 10 list for 2008 suggested people with diabetes might be harmed, not helped, by overly ambitious goals for blood sugar control (an HbA1c goal of below 6%).

Overdoing blood sugar control in the ICU might be harmful for several reasons. Low targets result in more episodes of extremely low blood sugar, or hypoglycemia, which can trigger a cascade of events with mortal consequences. The insulin used to achieve low blood sugar may have negative effects. Blood sugar control doesn't make the sugar disappear; it goes into cells. That surge of sugar may disrupt normal cell functions that wind up affecting the heart and other vital organs. Doctors aren't going to completely abandon controlling the blood sugar of ICU patients. But to paraphrase one commentator on the trial results, they'll now be looking for the "sweet spot" between control that is too tight and too loose.

8. CRP: Ready to make an entrance?

Late in 2008, results from the industry-funded JUPITER trial showed that people with normal LDL cholesterol levels (less than 130 mg/dL) but relatively high CRP levels (2 mg/L or higher) could cut their risk of having a heart attack or stroke in half by taking a high dose (20 mg) of a powerful statin drug, rosuvastatin (Crestor). CRP stands for C-reactive protein, a chemical in the blood that's a good indicator of inflammation. Statin drugs are taken primarily to lower LDL levels, but this was added proof that they also calm inflammation.

That first round of JUPITER results made a big splash, but it left room for debate about how CRP testing and lowering should fit into cardiovascular care. Subanalyses of the JUPITER data published in *Lancet* helped clarify if not completely settle matters. People in the trial who reached a very low LDL level (less than 70 mg/dL) cut their risk of having a cardiovascular "event" (heart attack, stroke, and so on) by 55%. But those who achieved a sub-70 LDL and a CRP of less than 2 mg/L lowered their risk by 65%. And reaching a CRP of less than 1 mg/L lowered it by 79%.

Many unanswered questions remain. What are the long-term consequences of taking high doses of potent statins like rosuvastatin? Might changes in diet, or increased physical activity, achieve the same thing?

Still, the JUPITER results add to the evidence showing that cardiovascular disease is fundamentally an inflammatory process. The official LDL-centric guidelines haven't changed, but many doctors are going ahead and ordering CRP tests for their patients with cardiac risk factors, even if their LDL levels are normal. If two tests show the CRP level is high, they may prescribe a high dose of a potent statin.

9. Screens with holes

Fresh doubts emerged about the wisdom of the current screening tests for breast and prostate cancers. A provocative analysis in *The Journal of the American Medical Association (JAMA)* came to the conclusion that the past 20 years of screening mammography for breast cancer and prostate-specific antigen (PSA) testing for prostate cancer has led to detection and treatment of many cancers that pose minimal risk while achieving only modest reductions in the number of more advanced cases. Earlier in the year, results from two large studies of PSA screening were equivocal.

The logic of cancer screening is impeccable: catch the disease early, while it's most treatable. The problems come when a test finds slow-growing, "indolent" cancers that could have gone untreated without causing harm but wind up getting treated anyway, so people needlessly suffer through the complications of treatment.

The American Cancer Society was sticking to its screening recommendations: women ages 40 and older should have annual mammograms, and men should discuss the pros and cons of prostate cancer screening with their doctors. But the group was reportedly working on public statements that would make people more aware of the pitfalls of screening. The authors of the *JAMA* article had several suggestions for how breast and prostate cancer screening could be improved: development of better tests that would differentiate between low- and high-risk tumors; more conservative treatment of low-risk tumors; targeting screening and prevention efforts at people in high-risk groups. They also suggested not calling low-risk tumors cancer, but referring to them as indolent lesions of epithelial origin, or IDLEs, instead. That rebranding might not catch on, but it's getting at the right idea.

10. Do your friends make you fat?

We know, we know: we gain weight because we don't eat the right foods and don't exercise enough to burn off the calories. But a new wave of research is showing that the causation of weight gain and a variety of other health-related behaviors has a social dimension, spreading through social networks as if they were contagious. Social networks are the vast webs of relationships we find ourselves in: friends and relatives; their friends and relatives, the friends and relatives of those friends and relatives, and so on.

Network analysis has roots in sociology, anthropology, mathematics, and several other disciplines. Dr. Nicholas Christakis, a Harvard Medical School professor, and James Fowler, a University of California political scientist, have applied the techniques from those fields to health-related issues. They started by painstakingly mapping out a social network based on information supplied by participants in the famous Framingham Heart Study. Their obesity findings in 2007 made headlines. In 2008, they used the same network to show how happiness ebbs and flows through social connections. They've popularized their ideas in a book titled *Connected*.

Their work has piqued people's interest partly because of some unexpected twists. For example, their obesity study found that your friend's obese friend may increase your chances of becoming

obese, even if your friend is not heavy. And in the happiness study, the happiness of friends seemed to rub off on people, but the happiness of coworkers did not.

How behavior could follow infectious patterns is uncertain, although Christakis and Fowler say subtle social messages of acceptance may get passed along from one person to another. Some say social network researchers are leveraging interesting correlations into causation. A related criticism is that network research has dressed up the time-honored observation that in social matters, like attracts like: clusters of behavior form because we are favorably disposed toward people who behave like we do. Regardless, viewing health-related behavior as a collective phenomenon is fascinating and opens up new avenues for research and experiments in intervention.

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