



DMS was recently awarded multiyear grants to study colon cancer prevention ( \$19 million), lung biology ( \$10.5 million), and the effects of exposure to toxic metals ( \$14.5 million).

## A case of “just say no” not working

Consider two drugs that relieve severe pain. There’s no evidence that either one works better or is safer than the other. But one is much more expensive. If tax dollars are buying one of these painkillers, which should it be?

**Alternatives:** Every day doctors prescribe controlled-release (CR) oxycodone (better known by the brand name OxyContin) instead of comparable but cheaper alternatives. Since state Medicaid programs often cover medications for low-income patients, several states have set policies to deter physicians from prescribing the expensive drug.

How well do such policies work? That was the focus of a study led by Nancy Morden, M.D., M.P.H., a family physician and outcomes researcher at Dartmouth. “For most drugs,” says Morden, prior authorization, the term for such policies, “is highly effective.” But, she and her co-authors reported in *Medical Care*, this drug seems resistant to prior authorization.

**Strict:** Between 2001 and 2004, 21 states implemented prior authorization for CR oxycodone. Twelve set strict policies, such as requiring a phone call from the physician. Nine had more lenient policies; the right phrase on a prescription might be sufficient. In the aggregate, strict policies

seemed to work better, resulting in a 34% drop in oxycodone use. Several states with lenient policies, however, saw an increase in use, and only a few saw a big decrease. Nationwide, CR oxycodone use among Medicaid beneficiaries grew 66% a year from 1996 to 2002.

In the end, the policies didn’t cut costs. On average, states saw only a 31¢ drop per daily dose of long-acting opiates—not much given the price gap between CR oxycodone and its alternatives. In 2004, the average wholesale cost of a daily dose of CR oxycodone was \$10.18, versus \$4.90 for sustained-release morphine and 45¢ for methadone.

**Cost:** “There are prescription drugs that really pay off in the short term and the long term,” says Morden. “There are prescription drugs that are maybe good for society but [that don’t] save money downstream, and that’s okay. . . . And then there are prescription drugs that just cost us . . . [that are a] waste of money.” Morden puts CR oxycodone in the last category.

She’s not sure why prior authorization didn’t work but thinks patients may be loyal to the OxyContin brand and doctors may resist restrictions on pain management. OxyContin’s value as a street drug may be a factor, too. And she and her coauthors believe misleading marketing plays a role. In 2007, OxyContin’s manufacturer was fined \$600 million and “pled guilty to a felony count of misbranding a drug with intent to defraud,” according to the Food and Drug Administration.

**Tax:** “How much of our money should we spend on oxycodone,” Morden muses, a note of frustration in her voice, “given that there is no literature to support it as being in any way at all superior to the generic cheaper products on the market? . . . Should your tax dollars pay for even one of these pills?”

**OxyContin’s value as a street drug may be a factor, says Morden.**

JON GILBERT FOX



Morden studied the effect of drug coverage policies.

### The truth about consequences

In a recent study of women with breast cancer, DMS researchers identified a puzzling consequence of invasive forms of the disease. There have been concerns for some time that powerful chemotherapy treatments can cause a decline in mental capacity. The DMS team wondered if maybe the cancer itself might affect cognitive performance before treatment even began. They showed in *Breast Cancer Research and Treatment* that this was, indeed, the case for some women with invasive breast cancer. Women with noninvasive cancer, however, did not suffer any pretreatment cognitive decline.



### Does change have the upper hand?

Not all change is for the better, concluded a study by DMS orthopaedist Kenneth Koval, M.D. He reported in the *Journal of Bone and Joint Surgery* that between 1999 and 2007, many early-career surgeons began using a different technique to treat broken wrists—without producing better outcomes. The shift from percutaneous fixation (in which the bone is aligned using pins inserted through the skin) to open treatment (an invasive procedure using screws or plates to set the bone) may, he said, reflect pressure “to offer new techniques to a medical market that is constantly searching for the latest in technological advancement.”





A team led by Michael Whitfield, Ph.D., has discovered distinct genetic profiles for different types of scleroderma, an autoimmune disorder that affects the connective tissues in the body.

## Parental example proves to be all-powerful

Children as young as two years old pay close attention to the food choices their parents make, according to a recent DMS paper. When preschoolers took a doll grocery shopping as part of a study, they “bought” food items that generally were as healthy—or unhealthy—as their parents’ purchases from real grocery stores. “Kids start forming their habits at a very young age,” says the paper’s lead author, Lisa Sutherland, Ph.D.

**Grocery store:** The researchers did a new analysis of data from a 2005 role-playing study initially conducted to evaluate the attitudes of 120 young children toward alcohol and tobacco. The children, who were between two and six years old, took a Barbie or Ken doll shopping in a miniature grocery store. In addition, their parents filled out questionnaires about their own food shopping habits. (For more on the 2005 alcohol and tobacco analysis, see [dartmed.dartmouth.edu/winter05/html/disc\\_barbie.php](http://dartmed.dartmouth.edu/winter05/html/disc_barbie.php).)

In the recent food-choice analysis, published in the *Archives of Pediatrics and Adolescent Medicine*, Sutherland and her colleagues classified the 47 food and beverage items in the pretend store as less healthy or more healthy.

Those with more added sugars and salt, such as cake and potato chips, were rated as less healthy than products such as fruit and milk.

**Junk:** “Most nutritionists would have suspected that kids fill their baskets with junk food when given the opportunity,” says Sutherland. In fact, about 11% of the children had shopping carts judged “most healthy” by the researchers; they had

chosen more than four healthy products for each less-healthy one. About 18% had carts judged “somewhat healthy.” And 71% had about equal numbers of more- and less-healthy items; their carts were judged “least healthy.”

It turned out that the only predictor of the healthiness of the children’s food purchases was their parents’ shopping habits. Kids with parents who reported buying healthier foods themselves were more likely to do the same in the pretend store. The finding may seem intuitive, says Sutherland. But “it’s the first time we’ve been able to show with a scientific study that at a very young age, children really mimic their parents’ [food choices].”

**Effect:** Factors such as age, gender, access to television, and parents’ education level appeared to have no significant effect on a child’s food choices. But, the researchers point out, a larger study might yield different results.

Sutherland, “a firm believer that parents have a huge impact on their children,” says parents can use their influence to help their children develop healthy eating habits. For instance, parents can allow their children to select which vegetables to buy for dinner.

They should also explain why products such as candy and soda aren’t very nutritious.

Yet even Sutherland, the mother of two, buys a popular but less-nutritious cereal every few months. When she does, however, she emphasizes to her children that it’s “not an everyday breakfast cereal for us” due to its sugar content. KATHERINE VONDERHAAR

**Even two-year-olds pay close attention to their parents’ food choices.**



### Web and the M.D.

Many doctors make less use than their patients do of web-based medical information. DMS researchers carried out a study of internet use by primary-care providers in Vermont and New Hampshire. “Studies suggest,” they wrote in *Family Medicine*, “that while patients want recommendations of online health resources from their providers, few receive them.” The researchers found that supplying providers with computers, high-speed internet access, and training did increase their use of web-based resources—but the doctors still remained loyal to other, less up-to-date sources of information.



### Pain in the brain

Glial cells are often overshadowed by neurons, their more famous neighbors in the nervous system, but they may be essential to an understanding of chronic pain. A group of DMS researchers reported in the journal *Brain Research* that two types of glial cells—microglia and astrocytes—play an important role in the onset and maintenance of long-term pain in rats. Chronic pain can be sparked by major surgery or cancer, among other causes, and current treatments are often ineffective or have serious side effects. The DMS team wrote that their work “may help in developing innovative strategies to treat chronic pain conditions.”





**DMS interventional radiologists found that in treating an aortic aneurysm from a blunt trauma injury, endovascular repair—done from inside the blood vessel—is better than surgery.**

## Ironing out a historical problem

In 1941, President Franklin Roosevelt faced a looming crisis: poor nutrition. Too many young men enrolling in the Army weren't getting enough vitamins and minerals, especially iron, in their diets. To produce hardier soldiers (and citizens), the government mandated that flour and bread be fortified with iron.

One result of this public-health intervention was a decline in anemia, which is caused by iron deficiency. But there may be some less-fortunate consequences.

**Lungs:** Iron performs many critical functions, including carrying oxygen from the lungs to the rest of the body. But humans use only a small amount of iron each day, so it accumulates—usually starting in the teen years for men and after menopause for women.

For years, researchers have hypothesized that iron might contribute to a number of medical problems, but few randomized trials have been done to confirm the connection. One of the few has been led by Leo Zacharski, M.D., a professor of medicine at DMS. Since 1999, he's studied iron levels and disease, including cancer, in 1,277 patients in a trial funded by the Department of Veterans Affairs.

**Levels:** Zacharski measured the amount of ferritin—a protein that stores iron—in all the patients' blood. Then about half of

them underwent periodic phlebotomies—or bloodletting—to reduce their iron levels. At the start of the trial, the average ferritin level for all participants was 122.4 nanograms of ferritin per milliliter of blood (ng/ml). The goal for those in the reduction group was to keep their ferritin levels between 25 and 60 ng/ml.

The results confirmed the concern about the risks of excess iron. Of the 641 patients in the control group, 60 developed new malignancies during the study and 36 died of cancer. In the reduction group, only 38 of 636 patients developed malignancies and 14 died of cancer—a statistically significant difference.

Further insight came from the fact that not everyone in the reduction group followed the study's guidelines. The intention was that they'd have their ferritin checked every six months and have a phlebotomy if it was over 60 ng/ml, but some patients waited longer than six months. Zacharski says this variability strengthened the finding, because patients who stuck to the schedule were less likely to develop a malignancy than those who did not. And in the control group, patients who developed malignancies had a higher average ferritin level than those who did not (127.1 versus 76.4 ng/ml).

Questions remain about how iron could cause cancer, but Zacharski is convinced of the connection. "Iron loves to react with oxygen," he says. Its affinity for oxygen is what makes it essential for proper cellular functioning. Extra iron, however, can produce molecules called free radicals, known to damage DNA, proteins, and lipids—a possible pathway to malignancy. So is it time to ditch a policy from a different era? Yes, argues Zacharski. For most Americans today, he feels, iron supplementation is unnecessary—and, in some cases, harmful.

**The results confirmed the concern about the risks of excess iron.**

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### Thinking about drinking

Between 1982 and 1988, the U.S. military set a drinking age of 21 on all U.S. bases and instituted programs to prevent alcohol abuse.

According to members of the DMS Department of Psychiatry, those efforts resulted in some dramatic changes. In a paper in *Military Medicine*, the team showed that

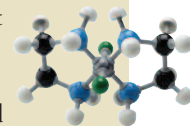
from 1992 to 2003, alcohol treatment rates dropped by 60% for young male veterans, compared with about a 25%



drop for the general male population during that period. The findings, they argue, support earlier work "suggesting that adolescent alcohol use, even in late adolescence, may contribute to later problem drinking."

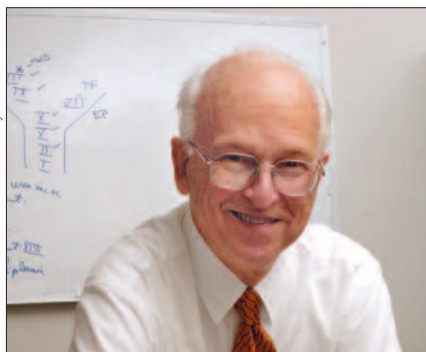
### Playing defense

The immune system is the body's best defense against the spread of cancer, but the system's dendritic cells actually play a role in *sustaining* tumor growth. Members of the microbiology and immunology department reported in *Cancer Research* that



targeting certain dendritic cells led to more effective treatment of ovarian cancer in mice. They found that depleting the number of dendritic cells made it harder for the cancer to spread and, surprisingly, strengthened the immune response. Used with standard chemotherapy, this technique "significantly delayed cancer progression." ■

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**Zacharski showed a link between iron and cancer.**