

For a **WEB EXTRA** with an interactive graphic of results from this study, see dartmed.dartmouth.edu/f09/we03.



A suspected whooping cough outbreak at DHMC was a false alarm. But the event had an upside in a finding that 88%-94% of vaccinated employees showed a booster response within just two weeks.

Are NCI centers the cream of the crop?

For decades, U.S. cancer centers have worked hard to attain and maintain National Cancer Institute (NCI) designation. But is there a measurable difference in the care patients get at the nation's 65 NCI-designated centers? Or is the designation merely window-dressing?

Until recently, no one knew for sure. But two recent studies, including one led by DMS researcher Tracy Onega, Ph.D., have finally shed light on the question.

The first study looked only at postsurgical mortality and showed short-term benefit to getting care at an NCI center.

Care: The DMS study, published in *Medical Care Research and Review*, was the first to look at both surgical and nonsurgical mortality. The researchers identified 211,048 Medicare patients who had cancers of the lung, breast, colon/rectum, or prostate diagnosed between 1998 and 2002. Then they compared mortality for 15,377 who got care at one of 15 NCI cancer centers to mortality for 195,671 who got care at non-NCI facilities. They reported on mortality one year and three years after diagnosis.

Mortality at one year was on average 25% lower in the NCI group than in the non-NCI group. And it was lower regard-

less of cancer type or stage at diagnosis. In fact, NCI patients with late-stage cancers had especially low relative mortality. Even NCI patients with three or more comorbidities (other health problems, such as congestive heart failure or diabetes) had 26% lower mortality at one year.

Outcomes: Just 7.3% of patients in the study got care at NCI centers. That means if all the patients had gone to NCI centers, there would have been over 4,000 fewer deaths at one year and over 2,000 fewer at three years. "This estimate, if extended to the entire population of cancer patients in the United States," the authors wrote, "could have major implications on cancer outcomes."

A surprising finding was that patients who had more primary-care visits than specialist visits in the six months prior to diagnosis had 22% to 28% higher mortality, compared to those who had predominantly specialist visits. The reason for this anomaly is unknown, Onega says.

Effect: The study had some limitations, including the fact that none of the 15 NCI-designated centers are in the southeastern U.S., so there's the possibility of a geographic bias. Even so, Onega believes the evidence is convincing that NCI centers offer an advantage. "When you look specifically at the people with high comorbidities who went to cancer centers versus those who didn't, the ones who went . . . did better," she says. "It's nice to see that even when you slice and dice and try to control and adjust for differences in the patient population . . . it still looks like the effect is there."

Next up is to find out why. The team suspects that high patient volumes, guideline-based treatments, and multidisciplinary care teams are possible reasons. "This is the first step," says Onega, "the 30,000-foot view." **MATTHEW C. WIENCKE**

Mortality at one year was on average 25% lower in the NCI group.

Let's talk about it

As talking heads nationwide argued about "death panels," a Dartmouth study showed that, when all treatment options have been exhausted, patients feel better if they talk about end-of-life issues. Patients with advanced cancer who got palliative counseling reported a higher quality of life and better mood than patients who did not. "Comprehensive, high-quality cancer care includes interdisciplinary attention to improving physical, psychological, social, spiritual, and existential concerns for the patient and his or her family," wrote Marie Bakitas, D.N.Sc., *et al.* in the *Journal of the American Medical Association*.



Vary important research

There are huge variations in the amount of health care provided per capita in different parts of the country, as DMS research has shown for years. But perhaps, critics have argued, those differences are the result of patient preference. According to a new paper by DMS and Dartmouth College experts, that's not the case. There are big variations in the intensity of care patients prefer, but those variations exist across the country. So, they argued in *Health Affairs*, "more of the variation in use is the consequence of health-care system characteristics than it is of patients' preference."



Dartmouth's Norris Cotton Cancer Center has been an NCI-designated cancer center since 1978.



DMS gastroenterologist Richard Rothstein, M.D., et al. reported in the *New England Journal of Medicine* on the effectiveness of a nonsurgical treatment for a precancerous esophageal condition.

The mind matters in disaster recovery

When major disasters like Hurricane Katrina strike, the damage to personal and public property is obvious. Less obvious, though often as devastating, is the effect on survivors' mental health. The Federal Emergency Management Agency (FEMA) has recognized the need for post-disaster mental-health support since 1974 by funding local crisis counseling programs (CCPs). But until recently, the programs had never been rigorously evaluated.

Fit: The CCP model has been "get in, [provide] support, and get out," says Jessica Hamblen, Ph.D., a DMS assistant professor and deputy director for education at the Dartmouth-affiliated National Center for Post-Traumatic Stress Disorder in White River Junction, Vt. "That does fit most of the time, until you have either extreme events or . . . events where most people do fine but . . . a subset . . . need more."

For several years, Hamblen has been developing an intervention for survivors who "need more." It was first used in New York City after 9/11; then in Florida after several major hurricanes in 2004; and in Mississippi after Hurricane Katrina in 2005. Hamblen published the Katrina results in April in the journal *Administration*

and Policy in Mental Health and Mental Health Services Research.

Data: CCPs are run "with a lot of good will," says Fran Norris, Ph.D., a DMS research professor and director of the National Center for Disaster Mental Health Research, who coauthored several papers in the same journal. "You probably won't meet many people who are more caring about their communities than people who get involved in disaster relief."

But good will doesn't provide usable data or evidence of value.

But good will and compelling anecdotes don't provide usable data or evidence of value. So Norris has been helping the agencies that oversee CCPs develop a system to collect standardized data.

Norris had planned to finish the evaluation system by 2006, but when Katrina struck in August 2005, she rushed to implement it. "I can't tell you how overwhelming this was," she says. For example, because Katrina evacuees ended up all over the country, Norris had to train the leaders of 19 CCPs in 18 separate conference calls. But now for the first time, researchers can assess CCPs.

For example, the data shows that "over a 16-month period, crisis counselors documented 1.2 million individual and group encounters across 19 CCPs," wrote Norris in one paper. Before, Hamblen says, CCPs "couldn't tell you basic things like how many people they served, what kinds of services they got, [or] who delivered the services." With a wealth of data now, Norris and Hamblen made recommendations in another paper for future CCPs.

Real: "Fran really understands the trade-off between asking the questions you want to ask . . . and [the] real world," explains Hamblen. "If you come up with a system that's too complicated . . ."

" . . . no one is ever going to do it," Norris concludes. She means to see that CCPs now "do it." JENNIFER DURGIN

Money isn't everything

For people with mental illness, steady employment offers more than a paycheck. A DMS research team evaluated the effects of holding a job on people with bipolar disorder, schizophrenia, and other serious conditions.

They found that those who were employed showed improvements in their mental health and made less use of outpatient services, saving the public about \$166,000 over 10 years. In *Psychiatric Services*, the researchers concluded that the "reduction appears to be dramatic, certainly enough to justify offering supported employment to all persons who use high levels of service and express interest in working."



DNA and diagnoses

To find out what genetic characteristics might predispose someone to bladder cancer, a group of DMS researchers studied mutations in the epidermal growth factor receptor (EGFR), an important regulator of the cell cycle. By comparing genetic variability in hundreds of people, both those with and without bladder cancer, they found that slight changes in the nucleotide sequence did seem to affect the risk of getting the disease. "Further confirmation of these relationships could help ultimately guide cancer prevention efforts or modify clinical care," they wrote in *Carcinogenesis*.



JON GILBERT FOX

Norris, left, and Hamblen are based at the VA.



Movie characters who smoke, regardless of whether they're "good guys" or "bad guys," influence teens to try smoking, according to a recent study led by DMS's Susanne Tanski, M.D.

Aiming a knock-out blow at malaria

By knocking out a key gene in the parasite *Toxoplasma gondii*, DMS researchers hope to strike a blow for global health. More than a billion people worldwide may be infected by *Toxoplasma*, which can cause damage to the central nervous system or death in infants and people with compromised immune systems. But the organism has added importance because it's a close relative of several other parasites, including *Plasmodium*, which causes malaria.

Model: David Bzik, Ph.D., a professor of microbiology and immunology, and Barbara Fox, a research associate in Bzik's lab, study *Toxoplasma* as a model organism that may help fight malaria and other diseases. In 2002, they created an attenuated, or weakened, strain of *Toxoplasma* that showed great promise as a vaccine. In a normal strain, Bzik says, even a single parasite can kill a mouse. But in the weakened strain, mice could withstand being injected with 10 million parasites. At the same time, the weakened strain prompted an immune response that protected the mice against infection by virulent strains of *Toxoplasma*.

But before the finding could be used, Bzik and Fox had to provide the exact sequence of the strain's genome. "The prob-

lem with the original attenuated strain . . . is that it's not defined genetically," Bzik says. "If you ultimately want to put anything into people, you have to have a genetic definition [of it] . . . and you have to show that it's safe and efficacious."

Genome: A peculiar behavior of the parasite frustrated Bzik and Fox's efforts. When *Toxoplasma* encounters foreign DNA, it randomly inserts that DNA into its genome in a process called nonhomologous end-joining (NHEJ), making it hard for scientists to manipulate the organism's DNA and target specific genes.

With their progress stymied, Bzik and Fox looked for a way to disrupt NHEJ. They thought it might be possible to identify—and knock out—a specific gene responsible for allowing *Toxoplasma* to exhibit this behavior. They spent a year trying without success to knock out the gene that produces the protein KU-70, part of the NHEJ pathway in other organisms. Then they tried it with another protein, KU-80, and found that the resulting strain of *Toxoplasma* was much less likely to exhibit NHEJ.

Bzik is excited by the possibilities opened up by the finding. "It's really a major breakthrough," he says. He explains that the immune response prompted by *Toxoplasma* is just what's needed to combat a host of diseases, including malaria, tuberculosis, HIV, and cancer. With the NHEJ problem solved, creating new strains of *Toxoplasma* for use against these diseases will be much easier.

Host: Shutting down the NHEJ pathway may also yield other dividends. "By taking a genetic approach to study what the parasite is doing to the host cell, we're actually going to learn a lot about the biology of our cells," Bzik says. "There's so much biological knowledge that can come out of this in the future." AMOS ESTY

"It's really a major breakthrough," says microbiologist Bzik.

JON GILBERT FOX



Bzik, left, and Fox manipulated *Toxoplasma's* DNA.

Got breast milk?

In some developing countries, as many as one-third of HIV-positive mothers may pass on the virus to their children through breast milk. But intriguing research has found that children are less likely to become HIV-positive if they're fed exclusively breast milk instead of a combination of breast milk and other foods. To discover what protection breast milk might offer, a DMS team examined interactions between breast milk and the virus in test tubes. "Our results indicate that breast milk contains innate factors that potentially inhibit infection with cell-free HIV," they wrote in the *Journal of Acquired Immune Deficiency Syndromes*.



A dash of cold water

In 2006, the U.S. Environmental Protection Agency lowered the safety standard for the allowable level of arsenic in public drinking water to just 10 parts per billion. But even that level of exposure, reported DMS graduate student Courtney Kozul, affects the expression of genes involved in the immune response in mice. The results of the study, Kozul *et al.* wrote in the journal *Environmental Health Perspectives*, showed that such exposure "can have significant effects on expression profiles in mouse lung and, more important, on the protein levels of many important immune mediators." ■

