MARK WASHBURN

Margaret Karagas has found intriguing connections between the use of certain painkillers and the risk of bladder cancer.

Long-term NSAID use may reduce bladder cancer risk

As an epidemiologist interested in the causes and prevention of cancer, Margaret Karagas, Ph.D., was intrigued by early reports suggesting that the use of nonsteroidal anti-inflammatory drugs (NSAIDs) might prevent the development of bladder cancer.

Bladder cancer is a very common urologic malignancy. While the prognosis is typically favorable, recurrences are common and progression in disease is possible. In northern New England, both the incidence and mortality rate of bladder cancer are higher than the national average.

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Karagas wants to know why that is and to determine whether aspects of diet, lifestyle, or other environmental factors might increase or reduce the occurrence of bladder cancer.

Her interest in cancer began during childhood. An aptitude for math and an early fascination with biology led to an interest in the wonders of the human body. When the beloved priest—a nonsmoker—of her family's Greek Orthodox Church died from lung cancer, she became interested in how someone with healthy habits could develop a cancer that is clearly linked to smoking.

"This tragic event sparked my curiosity about why some people developed cancer and other apparently similar people didn't," Karagas recalls. "Discovering the causes of disease enables us to find ways of preventing it," she says. Additionally, her work can reveal markers of cancer's progression and inform the treatment of patients.

In 2007, she and her colleagues published a population-based study conducted in New Hampshire on the relationship between cancer and analgesic usage. Painkillers containing a now-discontinued drug—phenacetin—are a known carcinogen and suspected of being related to bladder cancer. Participants who had taken phenacetin before its withdrawal from the market appeared to be at greater risk, but Karagas observed a reduced risk of bladder cancer among users of other NSAIDs, such as aspirin.

Based on these early findings, Karagas, a professor of community and family medicine at Geisel and co-director of the Cancer Epidemiology and Chemoprevention program at Norris Cotton Cancer Center, and her colleague, Richard Waddell, D.Sc., a research assistant professor of medicine at Geisel, were approached by the Intramural Program at the National Cancer Institute to collaborate and expand the project regionally to include Maine and Vermont.

In 2012, they began looking further for connections between analgesics and bladder cancer. Karagas also studied 39 genes related to NSAID metabolism and a newer class of NSAIDs known as selective cyclooxygenase (COX-2) inhibitors.

Findings from this study suggest regular use—and particularly regular use over 10 years or more—of ibuprofen may reduce bladder cancer risk in individuals carrying a gene variant related to NSAID metabolism. Expecting a similar trend for selective COX-2 inhibitors, the researchers instead observed an increased risk of bladder cancer.

Noting that further investigation is needed, Karagas warns against leaping to conclusions or making recommendations.

"A growing body of literature suggests certain NSAIDs may reduce risk of bladder cancer, particularly in individuals with specific genetic traits," she says. "NSAIDs are a worthy area of pursuit—they may also reduce risk for other diseases and cancers."

The results were published in the *International Journal of Cancer*.

Susan Green

SURVEY SAYS

Many doctors are skeptical that patients with CDI (an infection by the bacterium *Clostridium difficile*) would be willing to be treated with fecal microbiota transplantation (FMT). The treatment is both safe and effective, but it has an obvious drawback: the need to infuse a stool sample taken from a healthy donor into the patient. But Geisel researchers, led by several medical students, found in a survey that most people would be willing to consider FMT, despite the method of treatment. "Our data suggest that patients may be more ready and willing to accept FMT as a treatment alternative for CDI than previously assumed," the authors wrote in *Clinical Infectious Diseases*.

ALIGNING INCENTIVES

From 2005 to 2006, Medicare lowered the reimbursement rate for chemotherapy given in the last 14 days of a patient's life in recognition of the fact that such treatments are often unnecessary. According to research led by Carrie Colla, Ph.D., an assistant professor of TDI, the change in payment led to a decrease in use of chemotherapy in the last two weeks of a patient's life at doctors' offices. By contrast, at hospitals, where the connection between a chemotherapy treatment and a doctor's salary is less direct, the chemotherapy rate remained unchanged. Colla noted in the *Journal of Oncology Practice* that "these results suggest that payment reform may be used to better align appropriate incentives with better quality of care."