Different sets of guidelines weigh factors such as family history of cancer, age, and tumor characteristics. For example, guidelines issued in 2015 by the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors recommend germline sequencing in cases of renal cell cancer with clear cell histology only if the patient is younger than 50 at diagnosis, has bilateral or multifocal tumors, or has one or more close relatives with the same tumor type.

Kenneth Offit, MD, of Memorial Sloan Kettering Cancer Center in New York, NY, and colleagues suspected that applying an agnostic approach—concurrent germline and somatic analyses for all consenting patients—would pinpoint more individuals who might qualify for targeted treatments or whose relatives might benefit from preventive measures. The researchers therefore sequenced 410 genes in normal and tumor tissue from 1,040 patients, most of whom had stage III or IV cancers, including bladder, colon, ovarian, breast, and prostate tumors. They checked for germline mutations of 76 genes associated with hereditary cancer predisposition, including *BRCA1*, *BRCA2*, *ATM*, *CHEK2*, and *RAD51D*.

The scientists found that 182 patients carried cancer-predisposing germline mutations that were clinically actionable. For example, 44 of 62 cases of prostate cancer had clinically actionable inherited mutations that would not have been detected under existing guidelines, including 12 in highly penetrant genes like *BRCA1* and *MSH*. Overall, the actionable hereditary mutations found in 55.5% of these patients would not have been predicted otherwise by their family history or disease phenotype.

Certain ethnic backgrounds have increased rates of specific germline mutations, and adding ancestry as a criterion for screening increases the number of actionable mutations detected. For example, Offit and colleagues calculated that screening for mutations common in people of Northern European or Ashkenazi ancestry, such as alterations in *APC*, *MUTYH,* and *CHEK2*, would have identified an additional 44 patients in the cohort who have actionable mutations.

Offit notes that his team's strategy influenced treatment in some cases. Of the 182 patients with actionable findings, 132 had mutations in DNA repair genes. As a result, 11 patients began receiving PARP inhibitors, platinum-based chemotherapy, or both. These therapies were discussed with or are planned for another 27 patients. Germline screening results also spurred the researchers to offer genetic testing to the families of 29 patients. Had they followed current guidelines, they wouldn't have identified 13 of these families.

"Our agnostic sequencing clearly detected actionable mutations that would have been missed," says Offit. However, he cautions, it's too early to start rewriting the guidelines for germline testing "until there's been further validation of this approach."

"It's a pretty exciting paper," says Heather Hampel, MS, a licensed genetic counselor at The Ohio State University in Columbus who helped write the 2015 genetic testing recommendations. "It's difficult to know how many people we are missing" with current guidelines, she says. Given the declining costs for germline testing, guidelines may one day no longer be necessary, she adds. "It may be the beginning of an era in which all cancer patients get tested for hereditary cancer mutations when they are diagnosed." *–Mitch Leslie* ■

For more news on cancer research, visit *Cancer Discovery* online at http://cancerdiscovery.aacrjournals.org/content/early/by/section.

NOTED

The majority of Americans are unaware of key cancer risk factors, according to a national survey carried out by the American Society of Clinical Oncology (available at www.asco.org). Less than a third knew that obesity and alcohol consumption increase cancer risk; meanwhile, cell phones and caffeine were incorrectly identified as risk factors by 14% and 8% of those polled, respectively.

Stand Up To Cancer (SU2C) launched four "Cancer Interception" teams aimed at detecting lung cancer and pancreatic cancer as early as possible. The groups will receive a total of $16.6 million in funding from SU2C, the Lustgarten Foundation for Pancreatic Cancer Research, LUNGevity, and the American Lung Association. Their research efforts include testing new preoperative treatments to allow more patients with pancreatic cancer to achieve complete tumor resection, and developing a blood-based lung cancer interception assay that can be used in conjunction with low-dose CT scans.

The FDA launched an educational campaign about biosimilars, posting fact sheets and graphics to a new website aimed at helping health care professionals better understand of these products and their approval process (available at www.fda.gov).

Being overweight or obese is associated with 40% of all cancers diagnosed in the United States, the Centers for Disease Control and Prevention (CDC) reported (www.cdc.gov/vitalsigns/obesity-cancer). Two in three U.S. adults weigh more than recommended, the CDC noted, and more than half of Americans aren't aware that excessive weight increases the risk of at least 13 cancer types, including meningioma, esophageal adenocarcinoma, multiple myeloma, and colorectal cancer.

The FDA cleared Magnetom Terra (Siemens), a seven tesla (7T) MRI device, for clinical use. This is the first 7T system to receive clearance; it more than doubles the static magnetic field strength available for use in the United States, and will enable "better visualization of smaller structures and subtle pathologies that may improve disease diagnosis," the agency said.