

Tool Helps Predict *C. difficile*'s Risk of Recurrence

BY ROBERT FINN

Many patients with *Clostridium difficile* infection experience repeated bouts of the illness, and a rule has been developed to accurately predict a patient's risk of recurrence.

The prediction rule, which is simple to use, takes into account a patient's age, use of antibiotics, and severity of disease. The investigators demonstrated that the rule has a diagnostic accuracy of 72%.

These factors had been shown previously to be significant independent predictors of recurrent *C. difficile* diarrhea, wrote Dr. Mary Y. Hu of Harvard Medical School, Boston, and her colleagues. A fourth independent predictor—the serum level of antitoxin A IgG—appeared to reduce the accuracy of the rule.

The investigators derived the rule from a study of 63 patients hospitalized with *C. difficile* infection between January and May 1998. They validated the tool with data collected prospectively from 64 patients hospitalized between December 2004 and May 2006.

The rule assigns 1 point to each of the following characteristics: age greater than 65 years, disease judged to be severe or fulminant in intensity, and additional antibiotic use after the discontinuation of therapy for *C. difficile* infection. In the validation group, recurrence occurred in 7 of 19 patients scoring 2 points or

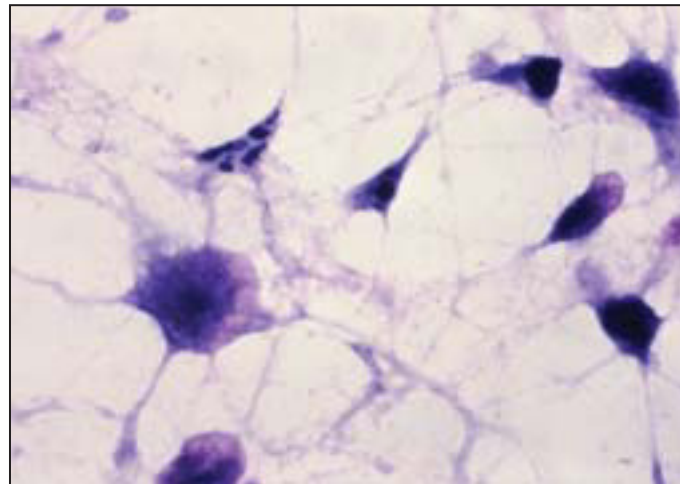
higher (37%) but in 6 of 45 patients scoring 0 or 1 (13%).

In the validation cohort, the sensitivity of the rule was 54%, the specificity was 77%, the positive predictive value was 37%, and the negative predictive value was 87%. The diagnostic accuracy was 72%. This compared favorably to the original derivation cohort, in which the rule's diagnostic accuracy was 77%.

If the rule's threshold for assigning patients to the high-risk group was changed to a score of 1 or higher, the sensitivity increased to 100% in the validation cohort, but the specificity decreased to 18%. "This alternative application may be useful in circumstances where high sensitivity is paramount," they wrote.

They also tested a combined rule that assigned an additional 2 points to a serum antitoxin A IgG level less than 1.29 ELISA units. With a threshold of 4 points or above, this combined rule appeared promising among the derivation cohort. Of these patients, 16 had antitoxin A IgG data available. Of those, all eight patients in the high-risk group had recurrent *C. difficile* infection, while only one of the eight patients in the low-risk group had recurrence. In this analysis, the sensitivity of the rule was 89%, the specificity was 100%, the positive predictive value was 100%, and the negative predictive value was 87.5%. The diagnostic accuracy was 94%.

Unfortunately, this rule proved to be



CDC/DR. GILDA JONES

A new rule can be used to predict recurrence of *C. difficile* infection, which can cause repeated bouts of diarrhea.

far less predictive in the validation cohort, in which 26 patients had antitoxin A IgG data available. Infection recurred in 3 of 6 patients in the high-risk group and 5 of 20 patients in the low-risk group. This translates to a sensitivity of 38%, a specificity of 83%, a positive predictive value of 50%, and a negative predictive value of 75%. The diagnostic accuracy was 69%.

The three-factor prediction rule for recurrence was "simple, reliable, and accurate," according to the investigators. "This rule is valuable in clinical practice as it defines a high-risk population in whom awareness of the risk can facilitate more

prompt recognition, diagnosis, and treatment of recurrent [*C. difficile* infection]. These patients are also most likely to benefit from interventions to prevent recurrence, such as infection control precautions, prudent use of antibiotics, prolongation of metronidazole or vancomycin therapy, and use of probiotics or other prophylactic measures."

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Digestive Diseases Cost More Than \$141 Billion Annually

BY MIRIAM E. TUCKER

The cost of digestive diseases in the United States now totals more than \$141 billion a year, according to a the National Institutes of Health.

In 2004, the number of digestive disease–related ambulatory care visits totaled 35 for every 100 U.S. residents, an increase of one-third since 1992. Also contributing to the \$141.8 billion total was an age-adjusted 35% increase in hospitalizations for digestive disorders between 1998 and 2004.

Those findings are among the data included a 192-page report by the NIH, *The Burden of Digestive Diseases in the United States*, a comprehensive compilation of statistics related to diseases that include GI cancers, infections, and functional disorders, as well as liver, biliary, and pancreatic disorders.

A series of three consecutive articles in the journal *Gastroenterology* summarizes certain aspects of the report, including the current state of medical care for GI disorders and the costs of that care. "Digestive, liver, and pancreatic diseases have a far-reaching medical, economic, so-

cial, and political impact on society in the United States and worldwide," said Dr. Anil K. Rustgi and Dr. Hashem B. El-Serag, respectively, editor and associate editor for *Gastroenterology* (2009;136:376-86).

In 2004, there were an estimated 72 million ambulatory care visits with a first-listed diagnosis of a digestive disease, and more than 104 million total listing a digestive disease. Digestive diseases were also common hospital discharge diagnoses, with approximately 4.6 million discharges of patients with a first-listed digestive disease diagnosis. A total of 4,608 of overnight hospital stays per 100,000 U.S. population had a digestive disease diagnosis in 2004, for a rate of nearly 5 per 100.

The recent 35% increase in overnight hospital stays with a diagnosis of digestive disease contrasts with a more modest 13% increase in hospital discharges for all diseases. In 1998, 25% of all hospital discharges had diagnoses of digestive diseases, compared with 30% in 2004. "Thus, rates of hospitalizations with digestive disease diagnoses increased both absolutely and as a proportion of

all hospitalizations," noted the report's editor, Dr. James E. Everhart of the National Institute of Diabetes and Digestive and Kidney Diseases.

In 2004, there were more than 236,000 deaths in the United States with a digestive disease as the underlying cause, representing 10% of all deaths. A gradual decline occurred in digestive disease mortality between 1979 and 2004, both as underlying cause (18%) and as underlying or other cause (20%). The greatest contributor to this decline was the decrease in digestive disease cancer mortality by 20% as an underlying cause and 24% as underlying or other cause.

The leading digestive disease diagnoses among ambulatory visits included gastroesophageal reflux disease (GERD), chronic constipation, abdominal wall hernia, hemorrhoids, diverticular disease, and irritable bowel syndrome, while the most common digestive disease-related diagnoses listed on hospital discharge records were GERD, diverticular disease, liver disease, constipation, gallstones, and peptic ulcer disease. The diagnosis of GERD has in-

creased severalfold in both ambulatory care visits and recorded hospital discharges since the early 1990s, Dr. Everhart noted.

The 10 most common prescription drugs from retail pharmacies for digestive diseases in 2004 included five proton pump inhibitors, accounting for 51% of all prescriptions and 77% of the total cost. Other costly medications included mesalamine, ranitidine, tegaserod, and ribavirin/peginterferon alfa-2a. A major deficiency in these data, derived from the Verispan database of retail pharmacy sales, is that they do not include nonprescription or alternative/complementary medications, infusions, mail-order drugs, or drugs given in the hospital, the authors said.

Direct costs for digestive diseases in 2004 totaled \$97.8 billion, of which hospital facility costs were the largest component, at \$40.6 billion. Diseases costing more than \$1 billion in facility charges included gallstones (\$4.3), abdominal wall hernia (\$3.5), and diverticular disease (\$2.2). Total physician charges associated with hospital services for digestive diseases were \$14.7 billion, of which only \$8.5 billion could be attributed to

individual digestive diseases. The most expensive of these were GERD (\$0.77 billion), gallstones (\$0.75 billion), and abdominal wall hernia (\$0.54 billion).

Total ambulatory care costs, including physician fees for office visits and in-office procedures, totaled \$16 billion. Expenditures for prescription drugs written by physicians during office visits were estimated to be \$12.3 billion, of which more than half was associated with drugs prescribed for GERD and peptic ulcer disease.

Of the \$85.7 billion in direct costs that could be attributed to individual digestive diseases, the six largest contributors were GERD (\$12.1 billion), gallstones (\$5.8 billion), abdominal wall hernia (\$5.7 billion), colorectal cancer (\$4.0 billion), diverticular disease (\$3.6 billion), and peptic ulcer disease (\$2.6 billion). As a group, cancers accounted for \$8.4 billion or 10% of the direct costs assigned to individual diseases.

The most costly diseases overall were liver disease (\$13.1 billion), GERD (\$12.6 billion) and colorectal cancer (\$9.5 billion).

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