When even people at high risk do not take up colorectal cancer screening

Uri Ladabaum

Despite the most intense efforts by medical professionals, a significant fraction of people who we believe ''should'' be screened are not being screened

Colorectal cancer (CRC) is a leading cause of cancer-related death in many parts of the world, including Europe, Australia and the USA. Screening is currently the most promising avenue to decrease the burden of CRC. The study in this issue of the journal by Bujanda *et al* (***see page 1714***)[1] serves as a sobering and instructive reminder of the challenges that many countries face in their efforts to establish CRC screening programmes, increase screening uptake and target higher-risk groups for more intense surveillance. Despite a dedicated effort to identify, contact and invite first-degree relatives of patients with CRC to undergo a colonoscopy free of charge (an effort that would be difficult to duplicate in many clinical settings), only 38% of these high-risk relatives who could be contacted agreed to undergo the procedure. What should we learn from this study, and in what context should we view the study's results?

GROUPS TARGETED

The relatives targeted for screening by Bujanda *et al* were divided into groups representing decreasing levels of CRC risk: those fulfilling Amsterdam II criteria, those fulfilling Bethesda guidelines and those with ''simple'' family history of CRC. The Amsterdam criteria emphasise CRC in multiple relatives and early age of onset, and were designed to be specific for identifying families with Lynch syndrome, while the Bethesda guidelines are meant to select patients most likely to benefit from further testing for Lynch syndrome. People with Lynch syndrome have a lifetime risk of CRC of up to 80%.[2] In Lynch syndrome, intensive surveillance has been shown to decrease CRC risk by 56% (10–78%), to decrease the risk of CRC death (0% vs 9% without surveillance) and to decrease the risk of death by 65% (1–88%) over a median follow-up period of 15 years.[3] People with one and two first-degree relatives with CRC have relative risks of developing CRC of approximately 2 and 3, respectively, compared with the general population.[4] Thus, one can estimate that the cohort studied by Bujanda *et al* included relatives with lifetime CRC risk ranging from 80% to 10%, depending on the details of the family history. These are people who would probably benefit from screening and who ''should'', by most doctors' judgment, be interested in CRC screening. Yet the majority declined it. Why?

FACTORS ASSOCIATED WITH SCREENING

The study by Bujanda *et al* was not designed to answer this question, but the authors examined factors associated with screening. After adjusting for other factors, age of the index patient of <65 versus $\geqslant 65$ years, a sibling or child relationship with the index patient versus a parent relationship, age of the relative of <65 versus $\geqslant 65$ years, and fulfilling the Amsterdam criteria versus the Bethesda guidelines were all associated with higher odds of taking up screening. The confidence intervals for most odds ratios were wide, reflecting the sample size of the study. Other factors associated with taking up screening were female versus male sex in the index patient and in the relative; it is not immediately clear how this should be interpreted. At first glance, one might feel reassured that these relatives as a group ''judged correctly'' that the potential benefit of screening was greater the more impressive their family history and the longer their own life expectancy. However, this study focused on a one-time invitation for colonoscopy, not the question of whether certain subgroups should have more aggressive surveillance than others. The disappointing finding is that a majority of relatives decided that it was preferable not to be screened at all, while the conventional medical viewpoint would be that most of them, barring serious comorbidities or very advanced age, would probably benefit from screening.

ADHERENCE TO SCREENING

Previous studies of families at high risk for CRC have also reported suboptimal screening adherence. In a study of families with classic or attenuated familial adenomatous polyposis, 54% of affected participants and 42% of at-risk relatives reported recent surveillance.[5] Genetic testing was not part of the study by Bujanda *et al*, but one study reported poor adherence with screening recommendations for mutation-negative people, who may have received false reassurance, in contrast with excellent adherence for carriers of mutations conferring high CRC risk.[6] In a study from the era before colonoscopic screening was widely accepted in the USA, only 42% of twin sisters of women with CRC had had a fecal occult blood test (FOBT) and only 16% had undergone sigmoidoscopy within a year of the report, although 89% had undergone at least one FOBT and 69% had undergone at least one sigmoidoscopy at some point in the past.[7]

SCREENING FOR PEOPLE AT AVERAGE RISK

Identifying high-risk subjects for more intense CRC surveillance is important, but CRC screening in average risk people is no less important, given that most CRCs are sporadic. Despite the public health impact of CRC and the effectiveness of screening, screening remains at low levels in many nations. In the USA, studies find that one half or less of the general population has been screened for CRC and a smaller fraction of the population currently undergo screening.[8–10] In recent years, a colonoscopic screening initiative has been launched in Germany, but the uptake rate was only 2% in the first year in Bavaria,[11] and the subsequent uptake has also been disappointing. In the study by Bujanda *et al*, only 4% of the relatives had already undergone colonoscopy at the recommendation of a doctor before they were contacted for the study.

In many countries, screening colonoscopy is not considered to be an acceptable or viable strategy for people at average risk, and efforts concentrate on other strategies, such as FOBT. FOBT enjoys the most robust evidence for reduction in CRC incidence and mortality,[12 13] but imperfect adherence even in clinical trials and the frequent failure to follow abnormal FOBT with a full colonic examination in clinical practice[14] exemplify factors that can prevent a screening strategy from fulfilling its potential benefit.

DETERMINANTS OF SCREENING BEHAVIOUR

The act of undergoing a CRC screening test is the culmination of a complex chain

of events involving many factors, including some related to the person being screened, that person's family and social surroundings, the doctors involved in the person's care, the healthcare system, and society at large. In the USA, the National Colorectal Cancer Roundtable concluded after a thorough literature review that the country needed to deal with several issues if it hoped to increase CRC screening rates, including patient and doctor barriers to screening, lack of universal coverage and incentives for adherence, and infrastructure needs.[15]

Patient perceptions, preferences and values influence CRC screening behaviour. Deterrents to screening colonoscopy include the bowel preparation, concern over adequate analgesia and embarrassment.[16] A study of patients referred for colonoscopy at a major university hospital found that half of the patients failed to complete the procedure.[17] Barriers to screening included lack of perceived risk for CRC, fear of pain, concerns about modesty and the bowel preparation, cost, other health problems, competing demands and scheduling challenges. One survey found that 43% of women in primary care prefer a woman endoscopist, that many of these patients would be willing to wait over a month for one and that a minority would be willing to pay more for one.[18]

A doctor's recommendation and shared decision-making are also important factors.[16 19 20] However, doctors' knowledge and implementation of CRC screening recommendations are not optimal, as highlighted by studies of internal medicine residents[21] and studies of practising doctors.[22]

In the USA, data from a large telephone survey suggested that the most important modifiable predictors of current CRC screening were healthcare coverage and a routine doctor's visit in the past year, highlighting the importance of access to care and perhaps attitude towards healthcare.[9] An analysis of US National Health Interview Survey data identified higher income, higher education, insurance coverage, a usual source of care and a dental visit in the past year as predictors of being up-to-date with CRC screening.[10] Lack of access to care should be a smaller barrier in countries with national health services, and it should not have been a major factor in the study by Bujanda *et al*. Nonetheless, all nations are likely to struggle with some problems of access. In Canada, it has been reported that male sex, higher income and higher educational level were associated with undergoing a screening colonoscopy versus a colonoscopy for other reasons.[23] Even if equitable access can be ensured, however, patient-specific factors will remain important. A retrospective study of 23 sites in a healthcare system found that doctor appointment-keeping behaviour was a predictor of attendance at a scheduled colonoscopy appointment.[24]

The complexity of the determinants of screening behaviour is illustrated by the study of families with classic or attenuated familial adenomatous polyposis by Kinney *et al*,[5] in which patient-related, doctor-related and healthcare system-related factors were associated with CRC screening patterns. In that study, the belief that CRC risk was not increased, lack of recall of provider recommendation for endoscopy, and lack of health insurance or no reimbursement for CRC surveillance were associated with not having a recent endoscopic evaluation.

Subtle forces relating to the societal perception of different diseases are likely to affect CRC screening patterns, but these are difficult to measure directly. Carlos *et al* examined data from the Behavioral Risk Factors Surveillance Survey and found that women who adhered to both mammography and Pap smear guidelines were more likely to adhere to CRC screening than whose who did not adhere to either gynaecological test, but these women's CRC screening rate was still only 52%.[25] Similarly, while adherence to prostate-specific antigen testing was the strongest predictor of CRC screening among men, only 65% of men tested for prostate-specific antigen underwent CRC screening.[26] Thus, even patients who adhered to screening for other cancers showed suboptimal adherence to CRC screening. Factors that are beyond the traditional realm of medicine and public health may prove more powerful than healthcare system-based initiatives. After the American celebrity Katie Couric's CRC awareness television campaign in March 2000, for instance, colonoscopy use increased in the USA.[27]

From the public health perspective, adequate resource allocation is imperative. The other edge of the CRC screening sword is the potential for overuse of tests, leading to maldistribution of resources. A study in Australia found that only 47% of patients referred for colonoscopy satisfied the National Health and Medical Research Council guidelines for colonoscopy on the basis of family history,[28] and another study reported that doctors recommended a significantly higher screening frequency than that endorsed in Australian guidelines.[29] A US survey found that a substantial fraction of primary care doctors recommended FOBT for patients <50 years old,[30] but it is difficult to know how the survey result relates to actual practice.

SUMMARY

In the multilayered challenge that is CRC screening, the study by Bujanda *et al* reminds us that despite the most intense efforts by medical professionals, a significant fraction of people who we believe ''should'' be screened are not being screened. What are we to do?

The various actors in this complex drama have different roles. Researchers must continue efforts to better understand CRC screening and to improve the relevant technologies. As doctors, we must assess our patients' risk, educate our patients and make sound recommendations given the current options. Some of us will personally deliver screening services. The medical and public health communities at large will help the individual practitioners by promoting efforts to increase public awareness and the societal acceptance of CRC screening. Payers including governments are responsible for funding the infrastructure to deliver screening. Ultimately, even if there were no barriers to CRC screening, patients will need to decide for themselves whether or not to be screened. We should strive to allow them to make an informed decision and to provide them with the ability to act based on this decision.

Gut 2007;**56**:1648–1650.
doi: 10.1136/gut.2007.125823

Correspondence to: Dr U Ladabaum, S-357, Box 0538, Division of Gastroenterology, University of California. 513 Parnassus Ave, San Francisco, USA; uri.ladabaum@ucsf.edu

Competing interest: None.

REFERENCES

1 **Bujanda L**, Sarasqueta C, Zubiaurre L, *et al*. Low adherence to colonoscopy in the screening of first-degree relatives of patients with colorectal cancer. *Gut* 2007;**56**:1714–8.
2 **Aarnio M**, Sankila R, Pukkala E, *et al*. Cancer risk in mutation carriers of DNA-mismatch-repair genes. *Int J Cancer* 1999;**81**:214–8.
3 **Jarvinen HJ**, Aarnio M, Mustonen H, *et al*. Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. *Gastroenterology* 2000;**118**:829–34.
4 **Fuchs CS**, Giovannucci EL, Colditz GA, *et al*. A prospective study of family history and the risk of colorectal cancer. *N Engl J Med* 1994;**331**:1669–74.
5 **Kinney AY**, Hicken B, Simonsen SE, *et al*. Colorectal cancer surveillance behaviors among members of typical and attenuated FAP families. *Am J Gastroenterol* 2007;**102**:153–62.
6 **Johnson KA**, Trimbath JD, Petersen GM, *et al*. Impact of genetic counseling and testing on colorectal cancer screening behavior. *Genet Test* 2002;**6**:303–6.
7 **Richardson JL**, Danley K, Mondrus GT, *et al*. Adherence to screening examinations for colorectal cancer after diagnosis in a first-degree relative. *Prev Med* 1995;**24**:166–70.
8 **CDC**. Colorectal cancer test use among persons aged > or =50 years—United States, 2001. *MMWR Morb Mortal Wkly Rep* 2003;**52**:193–6.
9 **Ioannou GN**, Chapko MK, Dominitz JA. Predictors of colorectal cancer screening participation in the United States. *Am J Gastroenterol* 2003;**98**:2082–91.

10 **Liang SY**, Phillips KA, Nagamine M, *et al.* Rates and predictors of colorectal cancer screening. *Prev Chronic Dis* 2006;**3**:A117.
11 **Birkner BR**, Kleff S, Thomas J, *et al.* Screening colonoscopy for colorectal cancer prevention: one year results from a prospective health care service research in Bavaria (Germany). *Gastroenterology* 2004;**126**:A348.
12 **Mandel JS**, Bond JH, Church TR, *et al.* Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. *N Engl J Med* 1993;**328**: 1365–71.
13 **Mandel JS**, Church TR, Bond JH, *et al.* The effect of fecal occult-blood screening on the incidence of colorectal cancer. *N Engl J Med* 2000;**343**:1603–7.
14 **Fisher DA**, Jeffreys A, Coffman CJ, *et al.* Barriers to full colon evaluation for a positive fecal occult blood test. *Cancer Epidemiol Biomarkers Prev* 2006;**15**:1232–5.
15 **Levin B**, Smith RA, Feldman GE, *et al.* Promoting early detection tests for colorectal carcinoma and adenomatous polyps: a framework for action: the strategic plan of the National Colorectal Cancer Roundtable. *Cancer* 2002;**95**:1618–28.
16 **Harewood GC**, Wiersema MJ, Melton LJ. A prospective, controlled assessment of factors influencing acceptance of screening colonoscopy. *Am J Gastroenterol* 2002;**97**:3186–94.
17 **Denberg TD**, Melhado TV, Coombes JM, *et al.* Predictors of nonadherence to screening colonoscopy. *J Gen Intern Med* 2005;**20**:989–95.
18 **Menees SB**, Inadomi JM, Korsnes S, *et al.* Women patients' preference for women physicians is a barrier to colon cancer screening. *Gastrointest Endosc* 2005;**62**:219–23.
19 **Janz NK**, Wren PA, Schottenfeld D, *et al.* Colorectal cancer screening attitudes and behavior: a population-based study. *Prev Med* 2003;**37**:627–34.
20 **Messina CR**, Lane DS, Grimson R. Colorectal cancer screening attitudes and practices preferences for decision making. *Am J Prev Med* 2005;**28**:439–46.
21 **Barrison AF**, Smith C, Oviedo J, *et al.* Colorectal cancer screening and familial risk: a survey of internal medicine residents' knowledge and practice patterns. *Am J Gastroenterol* 2003;**98**:1410–6.
22 **Klabunde CN**, Frame PS, Meadow A, *et al.* A national survey of primary care physicians' colorectal cancer screening recommendations and practices. *Prev Med* 2003;**36**:352–62.
23 **Bressler B**, Lo C, Amar J, *et al.* Prospective evaluation of screening colonoscopy: who is being screened? *Gastrointest Endosc* 2004;**60**:921–6.
24 **Turner BJ**, Weiner M, Yang C, *et al.* Predicting adherence to colonoscopy or flexible sigmoidoscopy on the basis of physician appointment-keeping behavior. *Ann Intern Med* 2004;**140**:528–32.
25 **Carlos RC**, Fendrick AM, Patterson SK, *et al.* Associations in breast and colon cancer screening behavior in women. *Acad Radiol* 2005;**12**:451–8.
26 **Carlos RC**, Underwood W, Fendrick AM, *et al.* Behavioral associations between prostate and colon cancer screening. *J Am Coll Surg* 2005;**200**:216–23.
27 **Cram P**, Fendrick AM, Inadomi J, *et al.* The impact of a celebrity promotional campaign on the use of colon cancer screening: the Katie Couric effect. *Arch Intern Med* 2003;**163**:1601–5.
28 **Yusoff IF**, Hoffman NE, Ee HC. Colonoscopic surveillance for family history of colorectal cancer: are NHMRC guidelines being followed? *Med J Aust* 2002;**176**:151–4.
29 **Olynyk JK**, Aquilia S, Platell CF, *et al.* Colorectal cancer screening by general practitioners: comparison with national guidelines. *Med J Aust* 1998;**168**:331–4.
30 **Richards C**, Klabunde C, O'Malley M. Physicians' recommendations for colon cancer screening in women. Too much of a good thing? *Am J Prev Med* 1998;**15**:246–9.

Autoimmune pancreatitis

Optimising corticosteroid treatment for autoimmune pancreatitis

Amaar Ghazale, Suresh T Chari

Unanswered questions

Autoimmune pancreatitis (AIP) is part of a systemic fibro-inflammatory disease that can involve multiple organs which characteristically have a lymphoplasmacytic infiltrate rich in IgG4-positive cells. IgG4-related systemic disease (ISD) has been proposed by Kamisawa *et al* as the umbrella term to describe this multi-organ disease.[1] Although the fibrosis in ISD can often lead to damage and even destruction of the involved organ, the inflammatory process typically responds to steroid treatment. However, the resolution of the inflammatory process in ISD may occur spontaneously without steroid treatment, especially in AIP.[2 3] The effect of steroid treatment on the natural history of AIP is not known as it is only recently that large series of AIP are being reported.

In this issue of *Gut* (**page 1719**), Hirano *et al*[4] report the results of a retrospective review of 42 AIP patients of whom 19 were treated with steroids. The authors' goal was to determine the effect of steroids on subsequent disease relapse by comparing "unfavourable events" in steroid treated patients with those in historical controls presenting before 2003 who did not receive steroids. "Unfavourable events" included the development of obstructive jaundice related to distal biliary stricture, sclerosing cholangitis with elevated liver enzymes, growing pancreatic pseudocyst or other extra pancreatic lesions that required treatment (retroperitoneal fibrosis, interstitial nephritis, sialoadenitis). "Unfavourable events" were less in the steroid treated group compared to controls (32% vs 70%, $p = 0.01$). The authors conclude that steroid treatment could reduce subsequent disease relapse and thus recommend the early introduction of steroids.

DEFINITIONS OF TREATMENT OUTCOMES

When discussing treatment in AIP, it is important to use specific terms that help identify treatment goals and responses. Remission refers to the resolution of disease-related symptoms and radiological abnormalities, whether spontaneously (spontaneous remission) or with steroids (steroid-induced remission), keeping in mind that in AIP, fibrosis-induced glandular and ductal distortion may prevent complete restitution of gland to normal architecture (and hence normal appearance on imaging). Induction of remission refers to the treatment of acute symptomatic and radiological manifestations of AIP with the goal of achieving disease remission. Maintenance treatment involves the use of immunosuppressive therapy to prevent disease relapse and maintain remission. Disease relapse is the recurrence of radiological manifestations of AIP (with or without symptoms) in the pancreas or extra pancreatic-involved organs. In the Hirano study,[4] most patients in the steroid group received long-term maintenance steroid treatment after initial disease remission. There are two questions that need to be addressed regarding steroid treatment in AIP: (1) what is the role of steroids in inducing disease remission at initial presentation and (2) is there a need for maintenance treatment to maintain remission and, if so, what is the most appropriate treatment?

MANAGEMENT OF THE ACUTE PRESENTATION OF AIP

Our understanding of the effects of steroid treatment in the acute phase of AIP is evolving. It appears that although spontaneous remissions do occur in AIP, the use of steroids brings about remission consistently and quicker than if no treatment were given. Steroids relieve disease-related symptoms (abdominal pain, obstructive jaundice) in most patients.[3] Concomitant with amelioration of symptoms, an improvement in radiological abnormalities is also seen with treatment. If there is any doubt about the diagnosis, the rapid response to steroids is reassuring and confirms the diagnosis. This includes resolution of pancreatic changes