Study 380 for a negative fecal occult blood test and with no family history of colorectal cancer, showed that if flexible sigmoidoscopy had been carried out alone, only 35.2% of women would have been identified for advanced neoplasia compared with 66.3% of matched men. The study is limited, however, by the fact that the flexible sigmoidoscopy findings are estimates.

In the authors' opinion, colonscopy is the preferred method of colorectal cancer screening in asymptomatic women of an average risk. These findings could have an important clinical impact, as colonoscopic screening is not currently widely used outside of the US.

Original article Schoenfeld P *et al.* (2005) Colonoscopic screening of average-risk women for colorectal screening. *N Engl J Med* **352:** 2061–2068

Diagnosis of the Lynch syndrome

Mutations in the mismatch repair genes *MLH1, MSH2, MSH6* and *PMS2* are associated with the Lynch syndrome (hereditary nonpolyposis colorectal cancer), with heterozygosity for a mutation conferring a strong propensity to cancer. As there is a need to improve diagnostic strategies for the Lynch syndrome, Hampel and colleagues investigated the frequency of these mutations in 1,066 patients with newly diagnosed colorectal cancer and compared the efficacy of two pre-screening methods for mismatch-repair deficiency.

Patients were genotyped according to five or six polymorphic markers in tumor and normal tissue to ascertain microsatellite instability. In total, 208 participants were classed as positive for microsatellite instability and were thus sequenced for *MLH1, MSH2, MSH6* and *PMS2* gene mutations, and underwent immunohistochemical staining and deletion analysis.

Of the 1,066 tumors, 135 had high-frequency microsatellite instability and 73 had low-frequency instability. Deleterious mutations leading to the Lynch syndrome were identified in 23 probands and the families of 21 of these patients were also screened, revealing Lynch syndrome mutations in 52 out of 117 relatives tested. Two probands were missed by both genotyping for microsatellite instability and immunohistochemical staining techniques.

In this study, the authors demonstrated the feasibility of large-scale screening of colorectal cancer patients and suggested that screening for mismatch-repair gene mutations by means of immunohistochemical analysis might be equally as effective as genotyping for microsatellite instability. The authors concluded that establishing the status of mismatch-repair proteins in colorectal cancer patients could have implications for prognosis and treatment of the condition.

Original article Hampel H *et al.* (2005) Screening for the Lynch syndrome (hereditary nonpolyposis colorectal cancer). *N Engl J Med* **352:** 1851–1860

Call for modification of the esophageal cancer staging system

Increasing numbers of patients with esophageal cancer undergo chemoradiation before surgery. The impact of this preoperative therapy has not, however, been defined as part of the standard esophageal cancer staging system used to assess long-term survival in these patients.

The esophageal cancer staging system currently incorporates tumor depth, nodal status and metastases status as factors for assessing overall survival. In their recent study, Swisher *et al.* retrospectively reviewed 593 esophageal cancer patients treated with or without chemoradiation and identified pathologic response to chemoradiation—defined in terms of amount of residual tumor remaining—as an independent predictor of long-term survival. The current staging system was updated accordingly: P0 = 0% residual, P1 = 1–50% residual, and P2 = >50% residual. The new system was found to predict survival at 3 years more accurately then pathologic stage alone ($P<0.001$). Furthermore, pathologic response was shown to be an independent factor even when controlled for pathologic stage ($P<0.01$). Pathologic response and nodal status were shown to be the most important predictive factors of long-term survival in patients treated with chemoradiation ($P=0.04$ and $P<0.01$, respectively).

The study purports to be the first to propose that chemoradiation is an independent risk