mutations. Conversion analysis confirmed the presence of all of these mutations, and also identified 12 large genomic deletions, an exon duplication and an exon mutation. This technique increased the diagnostic yield still further by revealing that 17 of the putative splice-site mutations resulted in splicing defects or affected mRNA transcript stability, and that 4 of the missense mutations resulted in exon skipping.

In summary, conversion analysis appeared to be superior to genomic DNA sequencing alone in the analysis of mutations in these colorectal cancer patients. Casey *et al.* note that the technique has now been adapted to use blood samples and so is feasible in a reference laboratory setting.

Original article Casey G *et al.* (2005) Conversion analysis for mutation detection in *MLH1* and *MSH2* in patients with colorectal cancer. *JAMA* **293:** 799–809

Zinc deficiency increases esophageal cancer risk

Animal studies have linked zinc deficiency to an increased risk of esophageal cancer, which is thought to be mediated by certain nitrosamines. This effect has been difficult to demonstrate in humans, however, because neither blood levels of zinc nor estimates of dietary zinc intake provide an accurate picture of the concentration of this mineral in the body's tissues. Abnet and co-workers have addressed this problem by measuring the concentration of zinc and other minerals directly in esophageal biopsy specimens, using X-ray fluorescence spectroscopy.

The samples were obtained from a population in Linzhou, China, where the diet contains large quantities of whole grain and little meat and therefore tends to be low in zinc. A total of 60 specimens were from subjects who subsequently developed esophageal squamous cell carcinoma during the 16-year Dysplasia Trial: 72 samples were from individuals who did not develop the disease. Baseline concentrations of zinc, copper, iron, nickel, and sulfur were measured by X-ray fluorescence at two sites within each tissue sample.

During the 16-year follow-up, participants in the highest zinc quartile were at a significantly lower risk of developing esophageal cancer than those in the lowest quartile (hazard ratio 0.21, 95% CI 0.065–0.680). The corresponding disease-free survival rates were 90% and 65% for the two groups, respectively, and the association was statistically significant across quartiles ($P = 0.015$). Sulfur concentration also appeared to be inversely related to esophageal cancer risk when the highest and lowest quartiles were compared, but this association was not significant across quartiles. None of the other minerals tested showed any such relationship.

In summary, the study provides evidence for the role of zinc deficiency in the development of esophageal squamous cell carcinoma in humans. The authors note that the approach described could be used to study other nutritional or toxic elements and their relationship with disease.

Original article Abnet CC *et al.* (2005) Zinc concentration in esophageal biopsy specimens measured by X-ray fluorescence and esophageal cancer risk. *J Natl Cancer Inst* **97:** 301–306

Do patient preferences reduce the validity of randomized trials?

Although a randomized controlled trial is generally accepted as the most effective way to assess clinical efficacy, patients' preferences for a particular treatment might affect the study's validity. This is particularly relevant when treatments are not blinded, and is likely to become increasingly important as patients take an ever more active interest in their management.

To assess the magnitude of any effect of patient choice on recruitment or outcomes, King and colleagues have carried out a systematic review of clinical studies that recorded patient or physician treatment preference. The selected studies followed up all participants, whether allocated to random or preference cohorts.

The results revealed that a considerable proportion of patients refused randomization because they preferred one treatment over another. In 14 of 27 studies included in the analysis, more than 50% of individuals refused randomization after having agreed to participate in the trial. Reassuringly, however, there was little bias in the characteristics of those who were randomized, and only small differences were found between the randomized and preference groups in terms of outcomes.