economic analyses will ultimately confirm or refute these observations.

It might be expected that response to treatment might influence survival. In a meta-analysis comparing the efficacy of intravenous 5-fluorouracil given by continuous infusion or by bolus, the overall response rates were 22% and 14% respectively (P = 0.0002); there was a survival advantage of 0.8 months for patients treated by infusion (12.1 months *v* 11.3 months, P = 0.04).[11] More recently, the same group explored the relation between response rates to various 5-fluorouracil regimens and survival.[12] This analysis evaluated data from 3791 patients enrolled in 25 randomised trials of standard bolus, single agent 5-fluorouracil, and experimental treatments (5-fluorouracil combined with folinic acid or methotrexate or infusions of 5-fluorouracil or floxuridine (5-fluoro-2'-deoxyuridine) through hepatic arterial infusion). The experimental regimens were associated with a 10.5% higher tumour response rate (P < 0.001), with an improvement in overall survival of about two months (P = 0.002). The overall survival benefit was a true function of the higher response rates obtained with the experimental therapy.[12] The more active the regimen (measured using tumour response as a surrogate) the greater the prolongation of overall survival.

Chemotherapy prolongs the time to tumour progression and the overall survival of patients with advanced colorectal cancer. These survival gains are accompanied by palliative benefits despite the potential toxicity of chemotherapy. Thus, there is now strong evidence to suggest that chemotherapy should be offered to all patients with advanced colorectal cancer, depending on their physical functioning. Patients should be allowed to make an informed decision, because only they can balance the modest gains in survival and improvements in quality of life from chemotherapy against the potential adverse effects of treatment.

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How to manage the first episode of schizophrenia

Early diagnosis and treatment may prevent social disability later

The lifetime prevalence of schizophrenia is about 1%, but the associated social disability and cost are disproportionately large. According to the World Health Organization, schizophrenia is among the leading causes of disability worldwide. Representative measures have estimated the annual cost of schizophrenia in England to be £2.6bn and in Canada to be $C2.35bn (£1.06bn).[1–3] A growing body of evidence suggests that the early stages of schizophrenia are critical in forming and predicting the course and outcome of the disorder.[4] Accordingly, clinical and research interest is now focused on the early stages of the illness because early detection and treatment may result in a better prognosis and functional outcome.

The first episode of schizophrenia typically occurs in the late teenage years or the early 20s.[5] However, the illness can remain undetected for about 2-3 years after the onset of clearly diagnosable symptoms.[4] Early recognition is hindered by the often insidious nature of the onset of schizophrenia, which occurs against a background of premorbid problems in language, cognitive ability, and behaviour.[5 6] Frequently, neurotic features (social anxiety, panic attacks, and obsessional ideas), antisocial behaviour, or substance misuse dominate the clinical picture and obscure the underlying psychosis.[5] Functional deficits such as emotional flattening, social withdrawal, and a lack of motivation and pleasure are usually prominent. The most commonly reported psychotic features are auditory hallucinations and delusions.

Once schizophrenia is diagnosed, the primary aim of treatment is to bring about rapid remission of the acute psychotic episode using the most effective and best tolerated drugs. A number of randomised clinical trials and cohort studies have suggested that patients are more responsive to treatment during their first epi-

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sode regardless of the antipsychotic drug used but are more sensitive to extrapyramidal side effects, such as acute dystonia and parkinsonism.[7] In this respect, treatment strategies that minimise the risk of side effects, such as the use of low dose typical neuroleptics or atypical antipsychotic drugs, may be a rational choice for the first episode.[7]

Although nearly 80% of patients with a first episode of schizophrenia will eventually recover, most (up to 70%) will have a second psychotic episode within five to seven years.[8] Early withdrawal of drugs is therefore not advisable. If drugs are to be discontinued, this must be done gradually, and plans should be made to enable the early detection and treatment of an impending relapse.[7] The emergence of a lack of response to treatment should also be addressed promptly. At present, clozapine is the only antipsychotic drug licensed in the United Kingdom for treating patients who have responded poorly to standard antipsychotic treatment.[7]

Even after clinical recovery, most patients have difficulty reintegrating into the community. They tend to underachieve in terms of education and employment and experience problems in forming relationships.[5] Intensive rehabilitation helps to minimise these social disadvantages at all stages of schizophrenia but may be particularly relevant in the early phase of the illness.[9] It is also important to work with the family to improve their knowledge of the condition and to nurture emotional relationships and communication between patients and their carers.[10] Cognitive behavioural therapy is useful in reducing persistent delusions and hallucinations, and cognitive remediation, a rehabilitation programme that targets cognitive impairment by teaching patients thinking skills, may provide the basis for improvement in social functioning.[11 12]

During their first episode of schizophrenia patients need specific services that provide rapid and easy access to specialist assessments, swift initiation of treatment in a setting which does not have stigma attached to it, and comprehensive psychosocial interventions and support. The development of close links between psychiatrists, primary care professionals, services for those who misuse substances, and educational and vocational services will help patients to be diagnosed early and allow them to benefit from continuing treatment and rehabilitation.

Focusing on early detection and intervention in schizophrenia offers the opportunity to make a real difference to the lives of our patients and their families. We cannot afford to miss it.

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Obesity surgery—another unmet need

It is effective but prejudice is preventing its use

Obesity, defined as having a body mass index >30 kg/m^2, is dramatically increasing in incidence in the Western world. For example, 20 years ago 5% of the population in the United Kingdom was obese; now 17% is.[1] The annual healthcare costs arising directly from obesity are at least £2bn ($3bn) in the United Kingdom and £45bn ($68bn) in the United States.[2 3] Data from several sources have identified the increased morbidity and mortality associated with obesity.[4] Most patients who are obese are treated with a combination of advice on diet and lifestyle and in some cases with drugs. However, for patients who have morbid obesity (body mass index >40), this conservative approach is doomed to failure.

If left untreated patients who are morbidly obese (1-2% of the population in the United Kingdom) have only a 1 in 7 chance of reaching their normal life expectancy. A Cochrane review in 1997 noted that good results had been obtained from surgery for obesity in these patients.[5] Over the past decade both the National Institutes of Health in the United States and the Scottish Intercollegiate Guidelines Network have suggested that surgery is the most effective treatment for selected patients who are morbidly obese; both organisations have recommended that surgery

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