followed by rapid weaning from breast milk may therefore provide the best approach until programmes to provide alternatives to breast milk are more fully implemented.[w6]

The recent policy debate considered whether a single age—for example, 6 months—would be appropriate as a global recommendation or if an age range would accommodate individual and regional variability better. It is important to separate recommendations for populations from those for individuals. A WHO expert consultation recommended exclusive breast feeding for six months, emphasising that this recommendation applies to populations while recognising that some mothers will be unable to, or choose not to, follow it.[11] In our view this recommendation is appropriate given the available evidence. A recommendation for an age range would be open to misinterpretation and commercial pressure from the infant formula industry. Evidence shows that exclusive breast feeding for six months is feasible and is acceptable to mothers in low income countries, as shown by the success of programmes promoting exclusive breast feeding and in the positive trends in the duration of exclusive breast feeding in many low income countries.[12 w7] At the same time means to ensure the adequacy of iron and zinc intake and to reduce HIV transmission in exclusively breast fed infants need to be sought.

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Competing interests: RB participated in a symposium sponsored by Nestle Corporation and co-edited a book on the proceedings of the meeting.

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Arrhythmias and sudden death in patients taking antipsychotic drugs

High doses and combinations of certain drugs are best avoided

The first report that patients with schizophrenia might be at special risk of arrhythmia and sudden death appeared in the early 1960s, when thioridazine was found to prolong the QT interval, an electrocardiographic abnormality that could lead to torsades de pointes and sudden death.[1–4] This same problem arose with sertindole—lengthening of the QTc interval and an apparent excess of sudden deaths in clinical trials—and led the US Food and Drug Administration to refuse it a licence.[5] Nevertheless, whether cardiac deaths are related to the illness itself or to the drugs used to treat it has remained unclear. Data from a very large American cohort of almost 100 000 outpatients with schizophrenia who were treated with antipsychotics were published recently and begin to suggest an answer: the drugs play a major part, although a risk factor conferred by the disease or associated with it may contribute (for example, smoking).[6] The study originated from unpublished preclinical work comparing ziprasidone, a new atypical antipsychotic drug that Pfizer had developed, with established antipsychotics. Ziprasidone caused notable QTc prolongation, and the FDA had concerns about licensing it mainly because of this abnormality.

The study examined administrative records (including all prescriptions) from three regions in the United States, comparing the incidence of cardiac arrest and ventricular arrhythmias and all cause mortality in patients with schizophrenia treated with an antipsychotic with that in two other cohorts, one with patients of glaucoma and one with patients of psoriasis. Both these conditions require long term medication, and neither is associated with cardiac risks. Of the patients with schizophrenia about 41 000 had received haloperidol, 24 000 thioridazine, 22 000 risperidone, and 8000 clozapine. With haloperidol, thioridazine, and risperidone the rate of cardiac arrest and ventricular arrhythmias and all cause mortality was two to five times higher than in the comparison groups. The findings confirm that all cause mortality in schizophrenia is relatively high. A dose-response relation could be identified only for thioridazine: the risk ratio for cardiac arrest and ventricular arrhythmias between the highest and the lowest doses was 2.5. In

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other words, the risk is greater with doses of thioridazine above 100 mg per day than with equivalent doses of haloperidol (3 mg or more).[7]

In practice it would be prudent to avoid doses of thioridazine over 100 mg per day and not to use the drug concurrently with any other that can lengthen the QT interval, such as erythromycin, azithromycin, and amitriptyline and other antidepressants—whether tricyclics or selective serotonin reuptake inhibitors.[8] The findings also call for a reassessment of the place of thioridazine in the management of schizophrenia. The relation of prolonged QT intervals to adverse outcomes remains uncertain. It seems certain, however, that adverse cardiac effects occur and can be mediated through cardiomyopathies, myocarditis, and other pathophysiological effects that might be expected to impair cardiovascular function.[9] Since at least some of these effects are likely to be dose related, it may be asking for trouble to use high doses—or different antipsychotics in combination. In the latest issue of *Current Problems in Pharmacovigilance* the Committee on Safety of Medicines emphasises the hazards of clozapine.[10] It recommends an electrocardiogram before treatment and close observation of all patients who develop persistent tachycardia during the first two months after starting treatment with the drug.

It is sobering to find that life expectancy for patients with schizophrenia may have fallen in recent years.[11] All these findings point to a need to pay more attention to the cardiac status of psychotic patients.

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Symptoms of possible oncological significance: separating the wheat from the chaff

The solution lies in a collaborative study of symptoms in the community

Symptoms are a common experience for all humans and are rarely synonymous with a particular disease. In the United Kingdom people are often encouraged to consult their general practitioner, and general practitioners are often advised to refer patients to secondary care according to the presence of one or more symptoms. Much of the evidence for this is based on the patterns of symptoms in patients with serious or important illnesses that are encountered by specialist clinicians.[1] The discriminant value of a symptom is related not only to the specific properties of that symptom but also to the characteristics of the setting and the population encountered.[2] An urgent requirement exists for attendance and referral practices to be based on data generated from epidemiological studies of symptoms in community settings.

Failing to respond to potentially serious illness accurately and efficiently can have adverse consequences for the delivery of high quality health care. Inaccuracy is about not identifying the true disease state resulting in false positive and false negative diagnoses. Inefficiency concerns the inappropriate or excessive use of tests or procedures beyond those needed to make a decision in a timely and cost effective manner.[3] For patients with cancer, false negative diagnostic inaccuracies and inefficiencies can have adverse effects on prognosis as well as the nature of the interventions required. Randomised controlled trials of screening for breast cancer and colorectal cancer have shown significant effects on mortality as a result of early detection of cancers.[4 5] In relation to patients with symptomatic breast cancer Richards et al have conducted a systematic review of the available literature in which, independent of the effects of lead time bias, delays of three to six months were shown to be associated with lower survival.[6] Furthermore, the EUROCARE high resolution studies have highlighted room for improvement in the pathological stage at which patients arrive at secondary care within the United Kingdom with consequent effects on cancer survival.[7] Delayed recognition of cancer as a result of inaccuracy or inefficiency may also lead to increases in distress and disability for the patient, in addition to the eventual need for more radical treatment.[8] For example, patients with late stage testicular cancer or cutaneous melanoma need more extensive and aggressive treatment than those with early stage disease.[9]

In relation to the approach to common symptoms of possible oncological significance in situations where

BMJ 2002;325:1254–5