women are tested, of whom 39 000 are aged 25-49.³ Switching to three yearly intervals means nine routine tests by age 50 instead of six. Allowing for the number already having tests for follow up, the actual change in workload for women aged 25-49 will be around 40%, or 15 500 additional women screened each year, together with consequent investigations, treatments, and counselling. At a conservative estimate, with liquid based cytology, of £25 (\$46; €36) per woman per year,⁴ this will cost an extra £385 000 each year.

The estimates from the commissioned case-control study² suggest this could at best add one woman to the existing 24 women annually (assuming proportional share of national benefit) in whom death from cervical cancer is prevented by our local programme.⁵ Given known problems with case-control analyses it could be less.⁶ With five yearly screening, for each death prevented at least 150 women have abnormal results, and at least 50 are treated.⁷ During any one year in Avon 3000 women aged 25-49 receive abnormal results.³ Changing to three yearly screening could add another 1000 women to this group.

So for districts efficiently regulating a five yearly programme the new policy requires diversion of £385 000 annually into an activity that possibly helps one, and adds 1000 to the "worried sick" category. If the NHS were flush with money and no more beneficial activities were in the queue needing funding then this would be acceptable. But there is no spare money and there are other unmet needs.

How unstoppable is three yearly screening? Avon dealt with it in 1987, described its approach in the *BMJ* in 1991,⁸ and has been cited as an example of good practice.⁹ During 15 years with a strict five year interval, returning non-indicated tests to the sender, we receive perhaps three queries a year from women, their partners, their members of parliament, or the press. We respond promptly, with a full explanation, and have never encountered disagreement. I have attended many meetings, seminars, and workshops with women's groups to discuss the issue. Always there is keen interest and real readiness to understand the prioritisation issues we face in health care.

The new guidance recommends no screening for women under 25. This is welcome, as the harm to benefit ratio makes screening unethical; for one woman who could be helped by screening in this age group there are tens of thousands who have abnormal results. Controlling this work will help offset the extra

cost of three yearly screening. Stopping routine screening beyond 50 would also help, but the NHS cervical screening programme has not sanctioned this. It takes 17 793 three yearly tests to detect one new high grade abnormality in well screened women over 50,¹⁰ and at most one death is prevented for each 36 high grades.⁷ To help one person older than 50 through routine five yearly screening therefore takes 420 000 tests, costing over £8m.

Suppose you are faced with the decision about investing £385 000 annually to benefit your local population. You can prevent one death every 22 years by routine five yearly screening beyond age 50, one death a year and harm an extra 1000 by switching to three yearly screening under 50, or 10 deaths a year through support that helps smokers stop,¹¹ and have enough spare to provide first rate nursing care and family support at home for 183 patients facing death from cancer.¹²

Which would you choose?

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NICE guidance on newer drugs for epilepsy in adults

Individualisation of therapy remains the key to successful treatment

With the introduction of felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate, vigabatrin, and zonisamide, the number of antiepileptic drugs marketed in different parts of the world has virtually trebled between 1989 and 2002.¹ The use of newer antiepileptic drugs is increasing steadily. In 2002 new antiepileptic drugs accounted for 20% of total prescriptions and for 69% of total costs for anti-

epileptic drugs in the United Kingdom (£99m of £142m).² Is the shift towards new antiepileptic drugs justified, and what are the indications for these drugs in the modern treatment of epilepsy? These questions are addressed in the latest guidance from the National Institute for Clinical Excellence (NICE).³

The guidance, which is based on data from randomised trials, other published information, and feedback from professional, specialist, patient, and

carer groups and drug manufacturers, focuses on the place of new antiepileptic drugs in adults. Zonisamide, not yet available in Europe, and felbamate—a last resort agent because of toxicity to bone marrow and liver—were not considered, but this does not affect the general applicability of the document. The conclusions reached are: firstly, monotherapy data in newly diagnosed patients do not show the existence of differences in effectiveness between newer and older antiepileptic drugs; secondly, although side effect profiles and interaction potential differ among drugs, adequate evidence does not exist to support the claim that newer drugs are generally associated with improved quality of life; thirdly, integrated cost effectiveness analysis shows a high degree of uncertainty about the costs and benefits associated with individual drugs; fourthly, seizure freedom, the most important outcome, is infrequently achieved during combination therapy in patients refractory to monotherapy, and insufficient evidence exists to determine whether any one of the newer antiepileptic drugs is superior to others in providing long term freedom from seizures. Overall, these conclusions agree with those reached in previous publications, including Cochrane reviews.^{1,3} Some of the studies showing improved outcome with newer antiepileptic drugs may in fact have been flawed by bias in study design or analysis.⁴

The guidance recommends that people with a first seizure be referred to a specialist for accurate diagnosis. If treatment is indicated (which is normally the case after two seizures have occurred), this should be initiated with a single drug, and combination therapy should be attempted only when at least two sequentially tried individual drugs have failed. Treatment should be monitored regularly and revert ultimately to the regimen (monotherapy or polytherapy) that proved most acceptable in terms of seizure control and side effects. As for the place of newer antiepileptic drugs, the guidance recommends that these be reserved for people who have not benefited from older agents such as carbamazepine or valproate. However, new antiepileptic drugs may be used as first line treatments when older antiepileptic drugs are contraindicated or are already known to be poorly tolerated by the individual, or when they are expected to interact with other drugs the patient is taking (most notably oral contraceptives) or when the patient is a woman of childbearing potential. In the latter situation, the guidance highlights the need for counselling on contraception (phenytoin, carbamazepine, barbiturates, oxcarbazepine, and felbamate reduce the efficacy of the contraceptive pill, whereas valproate, lamotrigine, gabapentin, lamotrigine, levetiracetam, tiagabine, vigabatrin, zonisamide and, at doses up to 200 mg/day, topiramate, do not⁵) and risks for the unborn child, specific caution being given against valproate because of risks for the unborn child.

The recommendations for women of childbearing potential are the most innovative. If a woman is taking (or planning to take) an oral contraceptive it makes sense to avoid enzyme inducers such as carbamazepine. The specific warning against valproate is stronger than in earlier guidelines,^{6,7} but may be justified by recent reports implying a greater risk of fetal malformations after prenatal exposure to valproate compared with monotherapy with other antiepileptic

drugs.⁸⁻¹² The latter findings, however, cannot be regarded as conclusive because of limited power in some studies and possible influence of confounders, and therefore evidence on which to base recommendations is far from ideal. Presumably, NICE also had to take into account the summary of product characteristics for valproate in the United Kingdom, which says that valproate should not be given to women of childbearing potential without specialist neurological advice and that for partial seizures it should be used only in women resistant to other treatments.

The NICE guidance is likely to have little impact on the trend favouring wider use of the newer antiepileptic drugs. As with all guidance, it will need to be adapted to local settings (including scarce resources in many countries), and it cannot substitute sound clinical judgment in individual cases. The guidance does not address the role of individual newer antiepileptic drugs, which differ in their tolerability profile and efficacy spectrum in specific epilepsy syndromes. The key to success in treating epilepsy is tailoring a drug's properties to the patient's characteristics,^{1,7} and in this respect newer antiepileptic drugs are welcome because they widen the range of options. The guidance is due for revision in 2006, when hopefully new evidence will be available from important studies, including pregnancy registries, and large randomised trials of newer and old antiepileptic drugs in newly diagnosed epilepsy (SANAD)² and in seizures with onset in old age (VA cooperative study #428).¹³

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