Prescribing selective serotonin reuptake inhibitors as strategy for prevention of suicide

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Abstract

***Objective*—To evaluate a policy to reduce the incidence of suicide by means of changing the prescribing of antidepressants from the older tricyclic antidepressants to the routine first line use of selective serotonin reuptake inhibitors or newer tricyclic and related antidepressants.**

***Design*—Cost effectiveness analysis with sensitivity analyses using observational data on costs, volume of prescribing, deaths, and toxicity.**

***Setting*—United Kingdom primary care.**

***Interventions*—Selective serotonin reuptake inhibitors or newer tricyclic and related antidepressants compared with the use of older tricyclics.**

***Main outcome measures*—Cost per life saved and cost per life year saved.**

***Results*—The potential number of lives which may be saved from a switch to the routine first line use of selective serotonin reuptake inhibitors is between 300 and 450 each year. The cost per life year gained ranges from £19 000 to £173 000, depending on the assumptions used. The cost per life year gained through the use of the newer tricyclic and related antidepressants is considerably lower.**

***Conclusions*—The cost per life year gained through avoiding suicides by the routine first line use of serotonin reuptake inhibitors is likely to be high. The new tricyclics and related drugs are of similar toxicity to the serotonin reuptake inhibitors but are considerably cheaper and so are more cost effective for this purpose. Further research is required on such prescribing. Because of the great uncertainties the shift to considerably more expensive options must be further investigated.**

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Introduction

There has been considerable debate over the past couple of years about the efficacy, effectiveness, tolerability, side effects, and role in the routine management of depression of a new class of antidepressants, the selective serotonin reuptake inhibitors.[1] Over this period there has been a rapid increase in prescribing these drugs, which now account for over 15% of the volume and 50% of the cost of antidepressant prescribing in the NHS.[2] Is this change in prescribing practice justified?

A recent meta-analysis of comparative clinical trials of selective serotonin reuptake inhibitors and tricyclic and related drugs found little difference in efficacy or overall drop out between the drugs.[3] Some of the claims of superiority for this class of drugs may therefore have been the result of selective reporting of more favourable trial results.

The principal claim now in favour of the use of these drugs as routine first line antidepressants is that they are safer in overdose and thus result in fewer deaths from suicide.[4,5] More enthusiastic supporters have even suggested that continued prescribing of tricyclics may be irresponsible,[6] unethical,[7] or negligent[8] because of the associated risk of suicide.

Deaths from poisoning with antidepressants account for around 7% of all cases of suicide and undetermined deaths, a figure which is consistent over time.[9] Exact rates vary depending on the definitions used, whether accidental deaths and open verdicts are included, and how deaths resulting from multiple drug ingestion are analysed. Therefore, a considerable reduction in the suicide rate due to antidepressant poisoning among people suffering from depression could have an important public health impact and help contribute to the *Health of the Nation* strategy, which calls for a 15% reduction in the suicide rate by the year 2000.[10] One of the strategies which the Department of Health proposes for decreasing the suicide rate is to reduce the availability of means by which suicide may be achieved because: "Reductions in access to easy means of lethal injury have been shown to have a marked effect on reducing suicides not compensated for by substitution of other methods."[11]

It is important, however, that policy on prescribing is based on estimates of the potential impact and costs of substituting selective serotonin reuptake inhibitors for other commonly used first line treatments. We examined the likely impact on suicide of a switch from current prescribing activity towards the use of selective serotonin reuptake inhibitors as the routine first line treatment in depression. We also studied the evidence on safety of antidepressants in overdose, the impact of changes in prescribing for depression on preventing deaths from suicide, and the direct costs associated with different patterns of prescribing antidepressants. We evaluated the prescribing of these drugs and considered the wide policy implications of the use of selective serotonin reuptake inhibitors as part of the public health strategy for mental health.

Methods

To estimate the number of suicides, related to use of antidepressants, deaths (whether deliberate, undetermined, or accidental) associated with each antidepressant for 1990 were obtained from data from the Office of Population Censuses and Surveys.[9] In about 30% of cases of fatal overdose with antidepressants more than one substance had been ingested, and the additional substances were most commonly other psychotropics.[12] Separate figures were obtained for all those deaths in which an antidepressant was involved in combination with other substances and those for deaths which were solely associated with an antidepressant.

To estimate the number of people (person years equivalent) ingesting each antidepressant, prescribing data for primary care in 1990 were obtained from the Prescriptions Prescribing Authority, Newcastle

(personal communication). Because of the potential inaccuracies in using the number of prescriptions as the basis of unit of treatment, prescribing data were combined with the defined daily dose tables of the World Health Organisation[13] to calculate the level of treatment for each antidepressant, expressed as person years at risk from each drug. The tables were supplemented with comparable estimates of appropriate daily doses in the few cases for which WHO estimates were unavailable. For reasons of (commercial) confidentiality the prescribing data may not be published on each drug individually and therefore only summaries and the results of the analysis based on data for individual drugs are reported here.

The toxicity of each drug and class of drug (older tricyclics, newer tricyclics and related antidepressants, selective serotonin reuptake inhibitors) as measured by the deaths by suicide per 1000 person years at risk was estimated by dividing the level of treatment by the number of deaths reported in the same year. These toxicity results were used in a model to estimate the cost per life year saved of a policy of prescribing selective serotonin reuptake inhibitors as the first line treatment for depression. The analysis was based on the optimistic assumption that no deaths from suicide are attributable to the ingestion of selective serotonin reuptake inhibitors; this is not in fact the case, but there are insufficient data with which to make precise estimates.

The 1992 costs of each drug were derived from *British National Formulary* prices.[14] After a recent reduction in the United Kingdom in the price of fluoxetine the cost of other selective serotonin reuptake inhibitors may also be expected to fall. Therefore, in this analysis it is assumed that there is a 25% reduction in cost of selective serotonin reuptake inhibitors as a group.

In the model a hypothetical cohort of the average population of people taking antidepressants this year is followed up over time. In one scenario current prescribing patterns are assumed to persist. In a second scenario it is assumed that patients are prescribed selective serotonin reuptake inhibitors in preference to the older tricyclic and related antidepressants, and the extra cost of this shift is calculated. The benefit from the policy in terms of life years gained is calculated by estimating the number of suicides avoided (effect rate × number of suicides) and their projected life expectancy by using life tables for the average population with the same age distribution as those committing suicide.

A proportion of those who are treated will relapse the following year (relapse rate). Some of these will be those for whom suicide was avoided in the previous year but who will commit suicide during relapse, so reducing the life years saved.

By calculating the life years gained and the costs of the two scenarios the incremental cost effectiveness of a shift from current prescribing patterns to prescribing mainly selective serotonin reuptake inhibitors for one year on that cohort can be generated. Various assumptions were used in the model. Firstly, we considered the percentage of current suicides related to use of antidepressants which may be prevented by the shift to selective serotonin reuptake inhibitors (effect rate). Some patients may use means other than their prescribed medication to commit suicide. The size of such a substitution effect is impossible to predict accurately (see discussion). Secondly, we included a relapse rate; the rate at which people after being treated with antidepressants in the first year will commit suicide in the subsequent year. Thirdly, we considered the criteria for attributing deaths to the antidepressant so estimating the potential lives saved by using a less toxic antidepressant. Finally, we included the life expectancy (mortality profile) of those in whom suicide is avoided.

We calculated the sensitivity of the estimates of the cost per life year gained to changes in the assumptions. The box shows the range of assumptions used in the model. All costs and benefits are discounted at the common rate of 5%, except where otherwise stated.

Assumptions used in model

- Relapse rate leading to suicide in those whose death was avoided in the first year of 0% (total recovery), 10%, or 20% applied to the second year of the analysis only
- Effect rate of selective serotonin reuptake inhibitors (% of antidepressant related suicides avoided) 20%, 40%, 60%, 80%, or 100%; 60% is taken as the middle estimate
- Selective serotonin reuptake inhibitors prices fall by 25% from 1992 prices
- Fatal toxicity rate of selective serotonin reuptake inhibitors is zero
- Criteria for attributing the suicide to the antidepressant is either that it is one of the drugs ingested in completed suicide (overestimate, 432 deaths) or that it is the sole drug ingested (underestimate, 298 deaths)
- The life expectancy of those in whom suicide is avoided is either the same as the average population of the same age or mortality is increased by two or three times

Results

There were 432 deaths reported in 1990 as result of poisoning with a substance or substances which included older tricyclic antidepressants and 298 deaths in which a single antidepressant was the only substance ingested; 161 deaths were associated with dothiepin hydrochloride and 89 deaths with amitriptyline hydrochloride alone. Newer tricyclic and related drugs were associated with eight deaths alone and 16 deaths in combination. There were no deaths attributable to selective serotonin reuptake inhibitors reported in 1990. By comparison 223 deaths were associated with paracetamol alone. Table I gives the relative toxicity of each drug taken alone or in combination. Table II

TABLE I—*Estimate of risk in overdose from different antidepressants*

Drug	Death rate per 1000* person years at risk: Taken alone	Taken in combination
Older tricyclics:		
Amitriptyline hydrochloride	0·703	1·042
Amoxapine	4·733	6·626
Clomipramine hydrochloride	0·247	0·494
Desipramine hydrochloride	2·215	
Dothiepin hydrochloride	0·683	0·920
Doxepin	0·513	0·820
Imipramine hydrochloride	0·572	0·875
Nortriptyline	1·870	2·805
Protriptyline hydrochloride		
Trimipramine	0·147	0·734
Weighted average for group†	0·663	0·961
Newer tricyclics and related drugs:		
Lofepramine	0·028	0·070
Matprotiline	0·679	1·019
Mianserin	0·178	0·415
Trazodone hydrochloride	0·252	0·252
Viloxazine hydrochloride	0	0
Weighted average for group†	0·084	0·168
Selective serotonin reuptake inhibitors:		
Fluoxetine	0	0
Fluvoxamine	0	0
Paroxetine	0	0
Sertraline	0	0

*Estimated weighted average across all prescriptions.
†Weighted for current prescribing levels in primary care in England (Prescriptions Pricing Authority)

shows the defined daily dosages and the costs of treatment with commonly used antidepressants.

By using a crude analysis and assuming that all deaths associated with older tricyclics are avoided by prescribing selective serotonin reuptake inhibitors, 432 lives could be saved in a year at a cost per life saved of nearly £370 000. If only those 298 suicides in which the antidepressant was the sole recorded cause of fatal poisoning are avoided the cost per life saved increases to over £500 000.

By using the cohort analysis the cost per life year gained can be estimated under a variety of assumptions (table III). The most favourable estimate of cost effectiveness is £19 412, assuming all 432 suicides are avoided with no relapse rate. Conversely, assuming only 20% of the 298 suicides are avoided with a relapse of 20%, the cost per life year gained is £172 908. By using a middle scenario of the effect rate (60%), the relapse rate (10%), and the number of suicides related to antidepressants avoidable (298) the cost per life year saved is estimated to be £51 717, with future benefits discounted at 5%.

TABLE II—*Estimate of cost of drug (£) treatments for depression*

Drug	Defined daily dosage (mg)*	Cost for 28 days†
Older tricyclics		
Amitriptyline hydrocholoride	75	1·31
Amoxapine	150	14·76
Clomipramine hydrochloride	100	7·71
Desipramine hydrochloride	100	3·99
Dothiepin hydrochloride	75	3·91
Doxepin	100	3·18
Imipramine hydrochloride	100	1·74
Nortriptyline	75	5·99
Protriptyline hydrochloride	30	3·08
Trimipramine	150	14·08
Weighted average for group‡		3·63
Newer tricyclics and related drugs:		
Lofepramine	105	7·48
Matprotiline	100	6·06
Mianserin	60	10·96
Trazodone hydrochloride	300	30·33
Viloxazine hydrochloride	200	7·11
Weighted average for group‡		9·11
Selective serotonin reuptake inhibitors:		
Fluoxetine	20	29·91
Fluvoxamine	150	35·00
Paroxetine	20	31·64
Sertraline	75	38·13
Weighted average group cost‡		31·36

*World Health Organisation 1992.
†Estimated weighted average across all prescriptions taking into account currently prescribed mix of preparation of each drug.
‡Weighted for current prescribing levels in primary care in England.

TABLE III—*Cost (£) per life year saved by prescribing selective serotonin reuptake inhibitors for prevention of suicide*

Relapse rate	Rate of effect of selective serotonin reuptake inhibitor				
	100%	80%	60%	40%	20%
Avoiding 432 suicides related to older tricyclic antidepressants					
0%	19 412	24 265	32 353	48 530	97 059
10%	21 405	26 757	35 675	53 513	107 026
20%	23 855	29 819	39 758	59 637	119 275
Avoiding 298 suicides related to older tricyclic antidepressants					
0%	28 141	35 176	46 901	70 352	140 704
10%	31 030	38 788	51 717	77 576	155 152
20%	34 582	43 227	57 636	86 454	172 908

The life expectancy of people whose suicide with antidepressants is avoided is unknown; it is, however likely to be lower than that in the population as a whole. If the above scenario is used but it is assumed that people whose suicide is avoided have twice the risk of death this figure rises to £57 912 (table IV).

The anayses indicate that the cost per life year saved is highly sensitive to assumptions on the potential number of suicides avoided and the effect rate of selective serotonin reuptake inhibitors in avoiding suicide; it is less sensitive to the rate of discounting

TABLE IV—*Cost (£) per life year saved under various assumptions*

No of suicides prevented	Relapse rate	Rate of effect of selective serotonin reuptake inhibitors		
		80%	60%	40%
Mortality two times higher than population				
432	0%	27 196	36 261	54 392
	10%	29 961	39 948	59 922
298	0%	39 425	52 567	78 850
	10%	43 434	57 912	86 867
Mortality three times higher than population				
432	0%	29 481	39 308	58 961
	10%	32 456	43 274	64 912
298	0%	42 638	56 851	85 276
	10%	46 941	62 588	93 882
Discount benefit at 0% per year				
432	0%	10 894	14 525	21 787
	10%	12 035	16 047	24 070
289	0%	15 756	21 007	31 511
	10%	17 447	23 262	34 893

TABLE V—*Selective serotonin reuptake inhibitors versus newer tricyclic and related antidepressants: cost (£) per life year saved for prevention of 432 suicides (298 suicides)*

Relapse rate	Rate of effect of serotonin reuptake inhibitors		Rate of effect of newer tricyclic and related antidepressants	
	80%	60%	80%	60%
0%	24 265 (35 176)	32 353 (46 901)	7747 (10 608)	10 330 (14 144)
10%	26 757 (38 788)	35 675 (51 717)	8543 (11 697)	11 391 (15 596)

future benefits, the relapse rate, and the all cause mortality of those in whom suicide is avoided.

Repeating the cohort analysis with a switch to the newer tricyclic and related antidepressants showed that this policy is considerably more cost effective than the switch to the selective serotonin reuptake inhibitors (table V).

Discussion

ESTIMATES OF TOXICITY

Determining the relative toxicities of different antidepressants in overdose is not easy. Because suicide is a rare event figures cannot be obtained from randomised clinical trials, but approximate relative risks can be estimated from routine observational data. One approach used has been to divide the number of deaths from suicide attributed to each drug by the volume of prescribing for that drug (from several sources) to yield a fatal toxicity index.[15] In the United States a similar approach has been adopted by using different data sources, and in addition a relative case fatality has been calculated for episodes of self poisoning from antidepressants.[16] League tables can then be constructed indicating the relative toxicity of each drug as judged by its association with cases of suicide.[17 18]

These must, however, be interpreted with caution as differences in the fatal toxicity estimates of antidepressants may also reflect the fact that different patients (with different risk of suicide) are prescribed different drugs.[16 19]

The most optimistic estimate of the reduction in the suicide rate which could result from prescribing selective serotonin reuptake inhibitors is 7% of the total or about 400-450 lives a year. This "best case" assumes that all fatalities in which there was any ingestion of an older tricyclic are attributable to properties of that drug and that selective serotonin reuptake inhibitors are not associated with any fatalities in overdose. In fact, the data are compatible with the selective serotonin reuptake inhibitors being of similar toxicity to some newer tricyclic and related drugs. For example, based on 1990 prescribing figures if the selective serotonin reuptake inhibitors had the same fatal toxicity as the older tricyclics then they would be associated with an average of 13 deaths

annually; if they had the same toxicity as newer tricyclics they would be associated with an average 1·7 deaths annually. The two suicides related to use of selective serotonin reuptake inhibitors reported for 1989 and 1991 are therefore compatible with these drugs being as toxic as newer tricyclics and related drugs.[2]

Although the selective serotonin reuptake inhibitors are relatively less toxic in overdose than the older tricyclic antidepressants,[20] it is the absolute risk of suicide associated with poisoning by different drugs which is important in determining health policy. Thus it is the small number of suicides associated with antidepressants which accounts for the high cost per life year associated with a policy of first line prescribing of selective serotonin reuptake inhibitors.

If the prescription of selective serotonin reuptake inhibitors could be targeted at patients who are at higher risk of suicide this would reduce the costs while maintaining most of the impact. It is, however, difficult to identify such high risk patients, and risk scalers may have a positive predictive value of less than 3%.[21-26] Therefore a routine first line prescribing strategy which aims to reduce suicide must be aimed at all patients receiving drug treatment, particularly in primary care, where about 90% of such prescribing takes place.

SUBSTITUTION WITH MORE LETHAL MEANS OF SUICIDE

The effectiveness of a policy of prescribing selective serotonin reuptake inhibitors in reducing deaths from suicide (effect rate) is difficult to predict but is likely to be considerably below 100%. This is because some people wishing to kill themselves may use a more lethal substitute. The importance of substitution of method of suicide is uncertain; it may be important enough to negate much of the benefit anticipated from prevention of public access to a lethal means of self injury.[27]

For example, deaths from carbon monoxide poisoning fell dramatically between 1962-3 and 1970-1, corresponding to a dramatic reduction in the proportion of carbon monoxide in domestic gas supplies.[28] The general downward trend in suicide rate, however, disguises the fact that suicide from all causes other than carbon monoxide poisoning increased slightly over the period, indicating at least some degree of substitution of method. The rate of suicide from motor vehicle exhaust poisoning, for example, has greatly increased in Britain since 1970 at a rate which cannot be explained simply by the growth in the number of vehicles on the road.[29]

The cost per life year gained from prescribing selective serotonin reuptake inhibitors increases substantially as the assumed rate of effect is allowed to fall.

EXCLUDED COSTS AND BENEFITS

Our economic analysis is partial in that it excludes a consideration of the likely cost of drugs dispensed to (though not take by) patients who drop out of treatment. The available evidence suggests that drop out from treatment for selective serotonin reuptake inhibitors and other commonly used first line treatments in depression are similar,[3] but there are no available data on the proportion who drop out after their prescriptions are dispensed. Drop out is likely to increase the cost of lives saved from routine first line treatment with selective serotonin reuptake inhibitors because of their greater cost. Similarly, as selective serotonin reuptake inhibitors are often prescribed with sedatives[3] it is unclear what the additional costs would be.

The most important cost element which has not been considered in this study represents the savings which may arise from the reduction in non-fatal suicide attempts. This may be considerable but we have not identified any serious studies which compare the costs of treatment episodes related to suicide attempts with different antidepressants. This topic needs more research.

HEALTH POLICY SHOULD BE BASED ON PROPER EVALUATION

The total cost of prescribing of antidepressants in primary care in England was around £88m in the year up to September 1992. If the trend towards prescribing selective serotonin reuptake inhibitors continues and the older tricyclics are completely replaced by prescriptions for these drugs the cost of antidepressant treatment will rise to over £250m in England.[2] If only 70% of the older tricyclics are replaced the total cost of treatment will increase to nearly £200m.

We have indicated that any benefit from increased use of selective serotonin reuptake inhibitors in terms of increased survival may be derived only at considerable cost and that the estimates of cost effectiveness are sensitive to assumptions about the effect rate, relapse rate, and numbers of suicides potentially avoidable. Rigorous research is required before sensible judgments can be made about important shifts in prescribing policy which have considerable fiscal implications. If a prescribing policy is to be used to reduce the number of suicides, a more cost effective policy may entail the use of the newer tricyclic and related drugs rather than selective serotonin reuptake inhibitors. This is because they are cheaper but with similarly low estimated toxicity.

Other interventions based reliably on randomised control trials show, for example, that the cost per life year of surfactant replacement treatment in severely distressed neonates is about £800 per life year,[30] and chemotherapy for advanced non-small cell lung cancer is just over £10 000 per life year.[31] Similarly, the deicision to adopt comprehensive breast screening strategies was based, at least in part, on an expected cost per life year saved of £5500 at 1991-2 prices,[32] although this value has subsequently proved unreliable.[33]

By using criteria developed in Canada it is uncertain whether prescribing selective serotonin reuptake inhibitors as a means of reducing suicide among depressed patients should be adopted.[34]

There are wider policy implications to this study. The *Health of the Nation* key area handbook on mental illness identifies changing the availability of means to suicide as an important part of the strategy to reduce suicide.[11] Such an unqualified policy seems to provide support to those in and outside the pharmaceutical industry who are keen to promote the routine first line use of selective serotonin reuptake inhibitor on grounds of safety. Alternative strategies aimed at high risk patients, such as those recently discharged from psychiatric inpatient care, which may be more cost effective are not explored.[35] In future the Department of Health should offer clearer guidelines on the most cost effective strategies for achieving its targets.

Antidepressant prescribing provides a further example of where the reasonable professional judgment of a clinician, when faced with an individual patient in the consulting room, is shown to be questionable on a population basis. On an individual basis the costs of suicide to the patient, the family, and the clinician who prescribes the antidepressant are high. From a social or population perspective, however, the costs of preventing suicide must be viewed within the context of the finite resources available and uncertainty of outcome. Thus there is a potential tension between the costs faced by individual general practitioners when deciding treatment for their patients and the costs faced by society. If practitioners

Clinical implications

- Selective serotonin reuptake inhibitors are increasingly being prescribed in primary care as routine first line treatment for depression
- Selective serotonin reuptake inhibitors are neither more effective nor better tolerated than other available antidepressants, many of which are considerably cheaper
- The potential number of lives which may be saved from a switch in prescribing to the routine first line use of selective serotonin reuptake inhibitors is between 300 and 450 each year
- The cost of avoiding suicides by prescribing selective serotonin reuptake inhibitors will be high
- Prescribing the newer tricyclic and related antidepressants as first line treatment for depression will have similar impact on rates of suicide but at considerably less cost

are to be advised against the routine first line use of selective serotonin reuptake inhibitors on the ground of uncertainty of the likely benefits and the high cost it is important that they understand the reasons for that advice and they receive support for the consequences of that policy.

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1 Edwards JG. Selective serotonin reuptake inhibitors. *BMJ* 1992;**304**:1644-6.
2 *The treatment of depression in primary care.* Leeds: University of Leeds, 1993. Effective Health Care Bulletin No 5.)
3 Song F, Freemantle N, Sheldon T, House A, Watson P, Long A, *et al.* Selective serotonin reuptake inhibitors: meta-analysis of efficacy and acceptabiity. *BMJ* 1993;**306**:683-7.
4 Montgomery SA, Lambert MT, Lynch S. The risk of suicide with antidepressants. *Int Clin Psychopharmacol* 1988;3(suppl 2):15-24.
5 British Association for Psychopharmacology. *Guidelines for treating depressive illness with antidepressants.* London: British Association for Psychopharmacology, 1992.
6 Montgomery S, quoted in: GPS unwittingly increase suicide risk. *General Practitioner.* 1992:May 22:68-9.
7 Milne S, Alcorn A, Bell A. Effective and acceptable treatment for depression. *BMJ* 1993;**306**:1126.
8 Fradd SO. Selective serotonin reuptake inhibitors [letter]. *BMJ* 1992;**305**: 366.
9 Office of Population Censuses and Surveys. *Mortality statistics.* London: HMSO, 1990.
10 Department of Health. *The health of the nation.* London: HMSO, 1992.
11 Department of Health. *The health of the nation key area handbook: mental illness.* London: Department of Health, 1993.
12 Farmer R, Pinder R. Why do fatal overdose rates vary between antidepressants? *Acta Psychiat Scand* 1989;**80**(suppl 354):25-35.
13 World Health Organisation. *Anatomical therapeutic chemical (ATC) classification index.* Geneva: WHO collaborating centre for drug statistics methodology, 1993.
14 British Medical Association and Royal Pharmaceutical Society. *British National Formulary Number 24 (September 1992).* London: BMA and RPS, 1992.
15 Cassidy S, Henry J. Fatal toxicity of antidepressant drugs in overdose. *BMJ* 1987;**295**:1021-4.
16 Kapur S, Mieczkowski T, Mann J. Antidepressant medications and the relative risk of suicide attempt and suicide. *JAMA* 1992;**268**:3441-5.
17 Henry J. A fatal toxicity index for antidepressant poisoning. *Acta Psychiat Scand* 1989;**90**(suppl 354):37-45.
18 Henry J, Antao C. Suicide and fatal antidepressant poisoning. *European Journal of Medicine* 1992;**1**:343-8.
19 Beasley C, Dornseif B, Bosamworth J. Sayler M, Rampey A, Heiligenstein J, *et al.* Fluoxetine and suicide: a meta-analysis of controlled trials of treatment for depression. *BMJ* 1991;**303**:685-92.
20 Anon. Selective serotonin reuptake inhibitors for depression? *Drug Ther Bull* 1993;**31**:57-8.
21 Roy A. Family history of suicide. *Arch Gen Psychiatry* 1983;**40**:971-4.
22 Pokorny AD. Prediction of suicide among psychiatric patients: report of a prospective study. *Arch Gen Psychiatry* 1983;**40**:249-57.
23 Fawcett J, Sheftner W, Clark D, Hedeker D, Gibbons R, Coryell W. Clinical predictors of suicide in patients with major affective disorders: a controlled prospective study. *Am J Psychiatry* 1987;**144**:35-40.
24 Diekstra RFW, van Egmond M. Suicide and attempted suicide in general practice, 1979-1986. *Acta Psychiat Scand* 1989;**79**:268-75.
25 Lin EHB, Von Korff M, Wagner EH. Identifying suicide potential in primary care. *J Gen Intern Med* 1989;**4**:1-6.
26 Goldstein RB, Black DW, Nasrallay A, Winokur G. The prediction of suicide. *Arch Gen Psychiatry* 1991;**48**:618-22.
27 Sainsbury P, Jenkins J, Levey A. The social correlates of suicide in Europe. In: Farmer R, Hisch S, eds. *The suicide syndrome.* London: Croom Helm, 1980:38-53.
28 Kreitman N. The coal gas story: UK suicide rates 1960-1971. *British Journal of Preventive and Social Medicine* 1976;**30**:86-93.
29 Clarke RV, Lester D. Toxicity of car exhausts and opportunity for suicide: comparison between Britain and the United States. *J Epidemiol Community Health* 1987;**41**:114-20.
30 Tubman TRJ, Halliday HL, Normand C. Cost of surfactant replacement treatment for severe neonatal respiratory distress syndrome: a randomised controlled trial. *BMJ* 1990;**301**:842-5.
31 Jaakkimainen L, Goodwin PJ, Pater J. Warde P, Murray N, Rapp E. Counting the costs of chemotherapy in a National Cancer Institute of Canada randomized trial in no small-cell lung cancer. *J Clin Oncol* 1990;**8**:1301-9.
32 Department of Health and Social Security. *Breast cancer screening.* London: HMSO, 1986. (Report to the health ministers of England, Wales, Scotland and Northern Ireland by working group chaired by Professor Sir Patrick Forrest.)
33 Clarke PR, Frazer NM. *Economic analysis of screening for breast cancer.* Edinburgh: Scottish Home and Health Department, 1991.
34 Laupacis A, Feeny D, Detsky AS, Tugwell PX. How attractive does a new technology have to become to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluations. *Can Med Assoc J* 1992;**146**:473-81.
35 Goldacre M, Seagroatt V, Hawton K. Suicide after discharge from psychiatric inpatient care. *Lancet* 1993;**342**:283-6.

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WAY WITH WORDS

Affect, effect

All writers have hang ups on *affect* and *effect*, so it's a safe bet that doctors (whose level of literacy is not high) will be confused too. A recent article in a journal that asked not to be named had no less than three examples of wrong usage in the space of a few paragraphs: ". . . only a small proportion of those at risk were *effected*"; "Sperm are also *effected* by alcohol . . ."; and ". . . fetal development can be *effected*." It serves the author right for being so *affected*.

The verb *affect* means to influence or alter the behaviour of someone or something; it produces an *effect* on an individual or object. *Affected* therefore indicates that a change has been produced as the result of a particular action—that is, has been *effected*. This logical argument can be used to ensure that the right word has been chosen. In human terms *affect* can signify to move or touch someone emotionally, while *affected* can also be disparaging (as indicated above), implying pretentious or shallow behaviour.

The noun *affect* (with emphasis on the first syllable when spoken) is virtually confined to use in psychiatry, meaning feeling, emotion, desire. A pity really because if we could talk about "affect and effect" we would have a useful aide memoire, though perhaps "cause and effect" conveys the sense just as well.

Everyone knows that *affection* denotes a kindly feeling, and would surely never dream of calling it *effection*. An illness is sometimes called an *affection* which at first sight seems odd because it is unlikely to be kindly, until one realises that in both cases an individual has been *affected*.

To *effect* means to bring about, cause, or accomplish. The action has been *effected* and if successful is said to be *effective*. The noun *effect* is the result or consequence of a particular action and can, of course, be beneficial or harmful. *Effect* can also indicate the impression made, for example, by or on an individual or by a work of art. It is used in science to describe natural phenomena, like the Doppler effect.

So what, you say. Why do we need a potted lesson in grammar? Because these words are commonly used, and misuse may seriously affect (alter) meaning. Consider the following piece of officialese:

"Consequent development of the act is *effected* by the requirement of central government to produce five yearly plans for primary health care services."

Do they really mean that or has someone got a letter wrong?—ALEX PATON, *retired consultant physician, Oxfordshire*