Psychological Medicine, 2001, **31**, 1203–1210. © 2001 Cambridge University Press
DOI: 10.1017/S0033291701004548 Printed in the United Kingdom

Deaths from antidepressants in England and Wales 1993–1997: analysis of a new national database

R. SHAH,[1] Z. UREN, A. BAKER AND A. MAJEED

From Sutton Hospital, Sutton, Surrey; Office for National Statistics, London; and School of Public Policy, University College, London

ABSTRACT

Background. The prescription of antidepressants has increased substantially over the last 10 years. It is therefore timely to examine trends in mortality associated with overdoses of antidepressants and to compare the relative mortality associated with different antidepressants.

Methods. Data were derived from a newly developed national database of deaths from overdose and poisoning in England and Wales between 1993 and 1997. Age and sex specific death rates associated with overdose and poisoning with antidepressants were calculated together with numbers of deaths per 100000 prescriptions of individual antidepressants.

Results. Twenty per cent (2503) of all deaths from overdose or poisoning were antidepressant related. The number of deaths increased by 18% between 1993 and 1997. Ninety-five per cent of deaths from antidepressants were associated with tricyclic antidepressants, particularly dothiepin and amitriptyline. Tricyclic antidepressants were associated with 5·3 deaths per 100000 prescriptions, 4·4 for monoamine oxidase inhibitors and 0·4 for selective serotonin reuptake inhibitors. Annual death rates were highest in men aged 30–44 years (18·2 per million) and women aged 45–59 years (14·8). Death rates from antidepressants were 2·5 times higher in the most deprived fifth than in the least deprived fifth of enumeration districts.

Conclusions. Antidepressants are an important cause of death from poisoning and overdose. SSRIs and newer antidepressants are associated with $<10\%$ of the risk of death than the older antidepressants. There is a strong association between area deprivation and deaths from antidepressants.

INTRODUCTION

Suicide from antidepressant overdoses has been a topic of controversy for many years, with suggestions that some tricyclic antidepressants (TCAs) should be withdrawn from routine clinical practice due to their toxicity in overdose (Milne *et al.* 1993). Others claim that the under-recognition of depression and under-utilization of antidepressants to treat depression are more important issues than concerns about the safety of drug treatment (Kelleher & Daly, 1992; Isacsson *et al.* 1997). TCAs continue to be widely prescribed and make up approximately 50% of antidepressant prescriptions in 1998 in England and Wales (Department of Health, 2000). Repeated studies however, have indicated that these drugs are commonly prescribed in primary care at ineffective dosages to treat depression (Donoghue *et al.* 1996; Dunn *et al.* 1999). Over the last decade, a 'defeat depression' campaign organized jointly by the Royal College of General Practitioners and Royal College of Psychiatrists has aimed to reduce the stigma associated with depression and increase diagnosis and treatment levels (Paykel *et al.* 1997).

There has been a two-fold increase in prescriptions for antidepressants in the United

[1] Address for correspondence: Dr Rajen Shah, SpR in Psychiatry, Locality 4, Cheam Resource Centre, 671 London Road, Cheam, Surrey SM3 9DL.

Kingdom (UK) between 1991 and 1998, with a 16-fold increase in prescriptions for selective serotonin re-uptake inhibitors (SSRIs) during the same period (Department of Health, 2000). Studies in Finland (Ohberg *et al*. 1998), Norway (Rettersol, 1993) and Australia (Battersby *et al*. 1996) suggested that an increase in antidepressant prescriptions in these countries led to a significant rise in the suicide rate from antidepressant overdoses. However, we do not know if a similar increase in antidepressant associated suicides has occurred in the UK.

In the past, trying to measure accurately the mortality associated with antidepressants has been difficult because national estimates of this mortality have been based on data, which have had a number of limitations. For example, the data were held only in paper format, making even simple analyses difficult to carry out. There was also very limited demographic information on patients dying from drug overdoses and poisoning.

Accurate information on the relative toxicity of different antidepressant drugs in routine clinical practice is important because these drugs are widely used, both by general practitioners and psychiatrists. Information is also needed on whether any patient subgroups are particularly at increased risk from antidepressant associated death. To help provide this information, the Office for National Statistics (ONS) has developed a new national database of deaths from drug overdose and poisoning. The database enables far easier identification and analysis of these deaths. Entries have been made with consistent spellings and with the addition of *British National Formulary* codes, the database also includes additional information from the coroner's certificate. In this paper, we use the new database to examine trends in deaths from antidepressant overdoses and poisoning in England and Wales between 1993 and 1997 and to compare the relative toxicity of commonly used antidepressants in routine clinical practice.

METHOD

Definition of deaths from overdose and poisoning

All deaths in England and Wales that are violent, unnatural, suspicious or unexpected, where the cause is unknown, or which may have been due to an accident or suicide, must be referred to the coroner for further investigation. Deaths where there was a suspicion that a drug was involved will thus be referred to the coroner, normally by a doctor or by the police.

Unless the coroner is satisfied that the death was due to natural causes a post-mortem will be carried out by a pathologist. Following the post-mortem the coroner will normally hold an inquest. After taking into account the pathologist's report and any additional information, such as police reports, the coroner will decide the cause(s) of death and give a verdict. The coroner certifies the death using Form 99. Part V of this form has to be completed for deaths due to accident or misadventure and the coroner also has the option to complete it for non-accidental deaths. Part V requires additional details of where and how the 'accident' happened.

The coroner's certificate is sent to the registration office for the district where the death occurred. The registrar registers the death using the information on the certificate, but does not receive reports by the pathologist or police. The ONS then receives from the registrar the information on the registration form, plus Part V of the coroner's certificate. The ONS codes all causes of death mentioned on the death certificate to International Classification of Diseases, Ninth Revision, (ICD-9) codes. (The Tenth Revision will be used from January 2001.)

ONS database of deaths from overdose and poisoning

Until 1992, figures on deaths from overdose and poisoning in England and Wales were extracted manually from registration forms. This was a cumbersome process and made more difficult as the drugs were listed exactly as recorded on the coroner's certificate. Thus, drugs could be listed under their scientific or brand name, and were often spelled incorrectly. Consequently, producing accurate information on deaths from overdose and poisoning was difficult, as was producing information by age, sex or area of residence.

Information on deaths occurring from 1993 onwards have been stored electronically. In 1999 the ONS developed a database of drug-related poisonings to facilitate investigation of these deaths and to aid the identification of specific

Table 1. *ICD-9 codes used to classify deaths from overdose and poisoning and* BNF *categories used in this study*

Code/category	Description
ICD9 code	
304	Drug dependence
305.2–305.9	Non-dependent abuse of drugs
E850–858	Accidental poisoning by drugs, medicaments and biologicals
E950.0–E950.5	Suicide and self-inflicted poisoning by solid or liquid substances
E962.0	Assault by poisoning
E980.0–E985.0	Poisoning by solid or liquid substances, undetermined whether accidentally or purposely inflicted
BNF category	
4.3.1	Tricyclics and related antidepressants
4.3.2	Monoamine oxidase inhibitors
4.3.3	New antidepressants
4.3.4	Other antidepressants

substances. The database contains all deaths in England and Wales where the underlying cause of death is regarded as resulting from drug-related poisoning, according to the current ONS definition. The ICD-9 codes used for this definition are listed in Table 1.

The database contains every mention of a substance recorded on the death certificate or mentioned by the coroner. All prescription drugs on the database have also been coded to *British National Formulary* (*BNF*) categories. These developments now allow information on the number of deaths associated with a specific drug to be extracted more easily than in the past. The new database also makes it possible to examine deaths in relation to other factors such as age, sex and other diagnoses recorded on the death certificate.

Data analysis

Information on all deaths associated with an antidepressant (*BNF* categories 4.3.1–4.3.4) was extracted from the database. This included age, sex, year of death, area of residence and details of drugs taken. Alcohol was not categorized as a drug in the analysis. Deaths associated with *BNF* categories 4.3.3 and 4.3.4 were combined into one category for the purposes of the analysis.

The Department of Health supplied information on the number of prescriptions for individual antidepressants dispensed in the community in England during 1993–7. This information was used with the number of deaths associated with each drug to calculate the number of deaths per 100000 prescriptions. Deaths occurring in Wales were excluded from this part of the analysis, as we did not have data on antidepressant prescribing in Wales.

National population estimates (supplied by the Office for National Statistics) were used to calculate annual age and sex specific death rates associated with antidepressants for the period 1993–7. The postcode of each patient was also linked to an enumeration district using a look-up table. Enumeration districts for England and Wales were ranked into five groups on the basis of their Carstairs Material Deprivation Score, from least deprived (group 1) to most deprived (group 5), and annual death rates calculated for each group of enumeration districts.

RESULTS

There were 12798 drug-related deaths between 1993 and 1997, of which 20% (2503) were antidepressant related. Ninety-five per cent (2389) of antidepressant related deaths were from tricyclic antidepressants (Table 2). In most deaths, an antidepressant was the only drug taken (73%, 1790), but this varied by antidepressant class. Tricyclic antidepressants were more likely to be taken alone (72% of cases) than monoamine oxidase inhibitors (47% of cases), and SSRIs and other new antidepressants (32% of cases). In 14 deaths, there was no information in the coroner's report on the actual antidepressant taken.

Antidepressant type and number of deaths

The majority of antidepressant related deaths were due to tricyclic antidepressants. The proportion of deaths mentioning these drugs

https://doi.org/10.1017/S0033291701004548 Published online by Cambridge University Press

Table 2. *Deaths associated overdose and poisoning from antidepressants in England and Wales*, 1993–1997

Type of antidepressant	Taken	Deaths	
		N	%
4.3.1 Tricyclic antidepressants	Alone	1732	72·5
	With another drug	657	27·5
4.3.2 Monoamine oxidase inhibitors	Alone	17	47·2
	With another drug	19	52·8
4.3.3 and 4.3.4 SSRIs and new antidepressants	Alone	31	32·0
	With another drug	66	68·0
All antidepressants	Alone	1790	71·5
	With another drug	713	28·5

Table 3. *Deaths associated with individual antidepressant and number of deaths per* 100000 *prescriptions in England*, 1993–1997

Drug	Number of deaths	Prescriptions (thousands)	Deaths per 100000 prescriptions	95% CI
Tricyclic and related antidepressants (*BNF* 4.3.1)				
Dothiepin	1247	16442	7·6	7·2–8·0
Amitriptyline	797	13015	6·1	5·7–6·6
Imipramine	119	2193	5·4	4·5–6·5
Clomipramine	62	2647	2·3	1·8–3·0
Nortriptyline	53	838	6·3	4·7–8·3
Trimipramine	52	1580	3·3	2·5–4·3
Doxepin	34	886	3·8	2·7–5·4
Lofepramine	32	4446	0·7	0·5–1·0
Desipramine	22	40	55·0	34·5–83·3
Trazodone	15	1207	1·2	0·7–2·0
Amoxapine	10	70	14·3	6·9–26·3
Mianserin	4	632	0·6	0·2–1·6
Maprotiline	2	131	1·5	0·2–5·5
Butriptyline	0	1	0	—
Viloxazine	0	6	0	—
Protriptyline	0	66	0	—
Monoamine oxidase inhibitors (*BNF* 4.3.2)				
Tranylcypromine	20	269	7·4	4·5–11·5
Moclobemide	8	215	3·7	1·6–7·3
Phenelzine	7	259	2·7	1·1–5·6
Isocarboxazid	1	50	2·0	0·1–11·1
Iproniazid	0	0·2	0	—
SSRIs and other antidepressants (*BNF* 4.3.3, 4.3.4)				
Fluoxetine	42	10011	0·4	0·3–0·6
Venlafaxine	17	587	2·7	1·7–4·6
Paroxetine	16	6465	0·2	0·1–0·4
Sertraline	12	2732	0·4	0·2–0·8
Fluvoxamine	7	454	1·5	0·6–3·2
Citalopram	3	404	0·7	0·2–2·2
Reboxetine	0	7	0	—
Mirtazapine	0	8	0	—
Tryptophan	0	15	0	—
Nefazodone	0	230	0	—

decreased slightly from 96% in 1993 to 93% in 1997. During the same period, there was a corresponding increase in the proportion of deaths involving SSRIs and other new antidepressants. Dothiepin was responsible for 50% (1247) of antidepressant related deaths during the study period and amitriptyline for a further 32% (797) of deaths (Table 3).

There were substantial differences in the risk of death from overdose and poisoning when

https://doi.org/10.1017/S0033291701004548 Published online by Cambridge University Press

Table 4. *Antidepressant-related deaths in England and Wales* 1993–1997*: rates per million by age, sex and antidepressant class*

	Tricyclics		Monoamine oxidase inhibitors		SSRIs and other new antidepressants		All antidepressants	
Age	Male	Female	Male	Female	Male	Female	Male	Female
0–14	0·2	0·5	0·0	0·0	0·0	0·0	0·2	0·5
15–29	10·9	8·8	0·0	0·0	0·4	0·4	11·3	9·2
30–44	17·4	13·9	0·2	0·3	0·5	0·5	18·2	14·5
45–59	13·4	14·0	0·1	0·4	0·5	0·8	14·1	14·8
60–74	5·1	9·2	0·1	0·3	0·4	0·4	5·5	9·8
⩾ 75	2·0	5·3	0·2	0·0	0·0	0·2	2·2	5·5
All ages	9·5	9·0	0·1	0·2	0·3	0·4	9·9	9·4

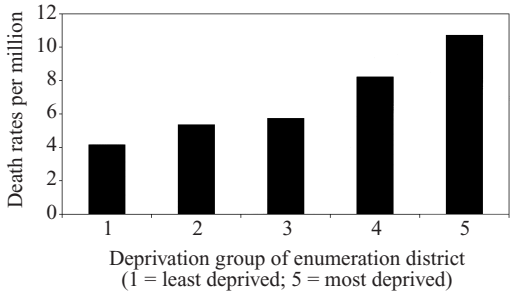

FIG. 1. Annual antidepressant-related deaths per million population by deprivation score of enumeration districts in England and Wales 1993–7.

deaths were compared with the number of prescriptions. Overall, tricyclic antidepressants were associated with 5·3 deaths per 100000 prescriptions, compared with 4·4 for monoamine oxidase inhibitors and 0·4 for SSRIs and other new antidepressants. Of the commonly used antidepressants, dothiepin (7·1 deaths per 100000 prescriptions) and amitriptyline (5·8 per 100000) appeared to be associated with the greatest risk of death. Lofepramine (0·7 per 100000) was associated with the lowest risk of death among the commonly used tricyclic antidepressants. SSRIs and other new antidepressants were associated with relatively low risks of death.

Time trends in death rates

The number of deaths per year increased from 459 in 1993 to 539 in 1997, an 18% increase. The highest death rate was in 30 to 44 year-old men (Table 4). Among people aged 15 to 44, death rates were higher in men than in women but among older patients, death rates were higher in women. In 1993, antidepressant related deaths were higher in women than men (9·2 *v.* 8·5 per million). Between 1993 and 1997, death rates increased more quickly in men and by 1997, death rates were higher in men than in women (11·4 *v.* 9·1 per million).

Association with area deprivation

There was a strong association between area deprivation and deaths from antidepressants. Annual death rates between 1993 and 1997 were about 2·5 times higher in the most deprived fifth of enumeration districts than in the least deprived (Fig. 1).

DISCUSSION

This study confirms that the older tricyclic antidepressants and monoamine oxidase inhibitors are associated with a substantially greater risk of death from overdose than the newer antidepressants. Among the tricyclic antidepressants, lofepramine was associated with a lower risk of death from overdose and poisoning than the more commonly used dothiepin and amitriptyline. The death rate was low with SSRIs; fluoxetine was not associated with a significantly greater risk of death than the other SSRIs. Hence, concerns about the risk of suicide in patients taking fluoxetine (Teicher *et al*. 1990) may simply have arisen because this is the most commonly used of the SSRIs and not because it is any more likely to lead to suicidal ideation.

Death rates from antidepressants increased by 18% (from 459/year to 539/year) between 1993 and 1997; this should be placed in the context of an over three-fold increase in prescriptions for these drugs during this period. Death rates were highest among men aged 30 to 44 years-old and by 1997 were higher in men than in women.

https://doi.org/10.1017/S0033291701004548 Published online by Cambridge University Press

There was also a strong association between death rates and deprivation, with a more than two-fold difference in death rates between the most deprived and least deprived fifths of enumeration districts.

Strengths and weaknesses of study

This is the first study of antidepressant related deaths to use the new national database of deaths from overdose and poisoning and overcomes many of the limitations of previous studies. These limitations included inaccurate estimates of the number of deaths associated with antidepressants and an inability to calculate age and sex specific rates. The study is also the first to examine the association between deprivation and deaths from antidepressants.

The main limitation of the study is that in about 28% of antidepressant-related deaths, more than one drug was taken and it can sometimes be difficult to determine precisely which of the drugs taken was the immediate cause of death, particularly as toxicology data was not available. Another limitation is that the toxicity data in Table 3 does not take into account possible differences in case mix between groups of patients. For example, if tricyclics are used more commonly in secondary care to treat the severely depressed, this could have lead to the toxicity of these drugs being overestimated, however, as SSRIs are known to be safer in overdose, it is more likely that this group of drugs are more likely to be prescribed to suicidal patients.

Strengths and weaknesses in relation to other studies

Henry *et al.* (1995) studied the fatal toxicity of antidepressants in the UK between 1987 and 1992. They found that amitriptyline and dothiepin caused 82% of deaths from overdose. Their study differed from ours in a number of aspects. It only included deaths from an overdose with a single antidepressant; it did not indicate the ICD-9 classification of deaths being studied; and did not analyse deaths by age, sex, or area. The only previous study of suicide from antidepressants that included demographic data found that women were 2·5 times more likely to use antidepressants to commit suicide than men (Battersby *et al.* 1996). The conclusions were limited, however, by the low sample size (68 cases). Ohberg *et al.* (1998) studied suicide rates from antidepressant overdose in Finland between 1990 and 1995. They also found that the proportion of suicides committed by use of antidepressants increased over the study period, from 5·6 to 8·4%. They found that 82% of suicides by antidepressants were committed by use of TCAs. Unlike our study, they did not include accidental or undetermined deaths, thus excluding many antidepressant related deaths.

Meanings, mechanisms and implications

Our study confirms that antidepressants are an important cause of drug-related deaths. We also found that the greatest increase in rates and highest death rates were seen in men aged 30 to 44 years. This was an unexpected finding, as the prevalence of depression is known to be higher in women. The rise in rates in men may be partly explained by a rise in antidepressant treatment in this group, particularly subgroups that have been found to be at higher risk of suicide, such as young men (Kelly & Bunting, 1998; McClure, 2000), drug addicts (Oyefeso *et al.* 1999) and the unemployed (Lewis & Sloggett, 1998).

There were large differences in the toxicity of different antidepressants. SSRIs and other newer drugs (*BNF* 4.3.3, 4.3.4) had less than one tenth the number of deaths per prescription than TCAs. The most toxic drugs were desipramine and amoxapine, but these were prescribed relatively infrequently and thus did not contribute significantly to total deaths. Kapur *et al.* (1992) analysed data from suicides as well as non fatal overdoses using antidepressants in the United States. They also found that desipramine had a significantly higher rate of death from overdose than other antidepressants. A possible reason for the toxicity of desipramine is that its metabolization by hydroxylation displays genetic polymorphism. Fast hydroxylators have much shorter elimination half-lives than slow hydroxylators. Consequently, slow hydroxylators may suffer more significantly from the toxicity of desipramine overdose (Spina *et al.* 1985). The two most commonly prescribed antidepressants, dothiepin and amitriptyline, both had a high number of deaths per prescription and thus caused most of the deaths. Their toxicity in overdose is probably due to a higher incidence of seizures and arrhythmias than from other drugs (Buckley *et al.* 1994).

Although SSRIs are generally thought to be safer in overdose than TCAs, some authors have questioned the significance of antidepressant overdose as a means of suicide. Jick *et al*. (1995) studied the risk of suicide among patients taking different antidepressants. They found several factors correlated with risk of suicide and after controlling for these factors, the risk of suicide was similar among the 10 antidepressants studies. They concluded that people who are determined to commit suicide will do so even if one particular means (drug overdose) is made less available. However, patients with a high risk of suicide may be more likely to be prescribed drugs less toxic in overdose. This appeared to be the case in the study of Jick *et al*., as patients prescribed trazadone, lofepramine and fluoxetine (all drugs known to be safer in overdose) had a substantially higher prevalence of previous antidepressant use, indicating severe or treatment resistant depression, and a consequently high risk of suicide. Furthermore, during the study period (1988–1993) SSRIs were newly introduced and expensive drugs, and their use was mainly limited as second-line drugs in patients at high risk of suicide.

Venlafaxine was found to have a substantially higher toxicity then other newer antidepressants (*BNF* 4.3.3, 4.3.4). This drug had ten-fold higher deaths per prescription than the least toxic drug, Paroxetine, and similar toxicity to some TCAs (clomipramine, trimipramine). There may be a number of explanations for this finding; venlafaxine was introduced during the time period of the study and was more widely used in secondary care than general practice, thus it may have been prescribed to a population more likely to be suicidal and take an overdose. Another explanation may relate to the drugs similar pharmacokinetic profile to TCAs, both drugs raise levels of serotonin and noradrenaline, high levels of noradrenaline following overdose may result in sympathetic nervous system overactivity and subsequent cardiotoxicity. There have been a number of case reports of venlafaxine overdose indicating its potential cardiac and neurotoxicity (White *et al*. 1997; Blythe & Hackett, 1999).

The study results indicated a strong link between area deprivation and deaths. Durkheim (1952) recognized the importance of social deprivation in influencing suicide, and studies repeatedly indicate that the most socially deprived areas have highest suicide rates (Lewis & Sloggett, 1998; Whitley *et al*. 1999) and prevalence of depression (Blazer *et al*. 1994; Meltzer *et al*. 1995). Our results may be explained by, a higher prevalence of depression in deprived areas resulting in greater prescriptions of antidepressants and thus higher likelihood of these drugs being taken in overdose. Geographical variations in prescription habits, may be a further factor influencing death rates, areas where patients are prescribed TCAs more frequently may have higher death rates from overdose.

There is evidence that restricting the means of suicide decreases suicide rates. In the United Kingdom, reductions in suicide rates resulted from the decrease in barbiturate prescriptions and the change in the domestic gas supply (Office of Health Economics, 1981). In the case of antidepressants, restricting the availability of drugs that are toxic in overdose may prevent the deaths of the many people who take accidental or impulsive overdoses. It would also buy time during which the suicidal impulse may pass and allow the patient to come to the notice of psychiatric services. Assuming method substitution does not occur on a large scale, withdrawing dothiepin and amitriptyline could result in the saving of up to 400 lives per year. However, a decrease in the prescription of cheaper TCAs, and an increase in the use of the higher priced SSRIs and lofepramine, would result in higher prescribing costs. Freemantle *et al*. (1994) in a cost effectiveness analysis of switching from older TCAs to SSRIs found the cost per life year gained would be high. However, this study did not take into account indirect costs of suicide (such as the loss of earning potential), the recent advent of cheaper generic SSRIs, or the costs of hospital treatment of overdoses (i.e. time spent in ITU).

Deaths from antidepressant overdose account for a small proportion of overall suicides but a much higher proportion of suicides in those being prescribed an antidepressant. One estimate is that the proportion of suicides from antidepressant overdose among depressed patients prescribed an antidepressant may be as high as 50% (Henry, 1997). Therefore, any increase in prescribing the more toxic TCAs will lead to an increase in suicide rates from overdose of these drugs. A recent Cochrane Collaboration review

found no clinically significant differences in the effectiveness of SSRIs and TCAs (Geddes *et al*. 2000). Hence, the prescription of TCAs cannot be justified by on the grounds of greater efficacy. Our findings suggest that policy makers should consider steps to reduce the prescription of the TCAs toxic in overdose, and encourage the prescription of newer antidepressants, particularly in groups at high risk of suicide.

Unanswered questions and future research

This study did not attempt to examine the cost-effectiveness of prescribing SSRIs and other less toxic antidepressants in place of older antidepressants. The new database of deaths from overdose and poisoning could help facilitate such a study. The database can also be used to carry out ecological studies examining the effects of changes in prescribing practice or public health policies on the risk of death from antidepressants. The database will be updated annually and will provide valuable data to help answer these and other research questions.

The development of the new national database of deaths from drugs and poisoning was funded by the Office for National Statistics. Azeem Majeed holds an NHS National Primary Care Career Scientist Award and is funded by the NHS Research and Development Directorate.

REFERENCES

Battersby, M. W., O'Mahoney, J. J., Beckwith, A. R. & Hunt, J. L. (1996). Antidepressant deaths by overdose. *Australia New Zealand Journal of Psychiatry* **30**, 223–228.

Blazer, D. G., Kessler, R. C., McGonagle, K. A. & Swartz, M. S. (1994). The prevalence and distribution of major depression in a national community sample: the National Comorbidity Survey. *American Journal of Psychiatry* **151**, 979–986.

Blythe, D. & Hackett, L. P. (1999). Cardiovascular and neurological toxicity of venlafaxine. *Human and Experimental Toxicology* **18**, 309–313.

Buckley, N. A., Dawson, A. H., Whyte, I. M. & Henry, D. A. (1994). Greater toxicity in overdose of dothiepin than of other tricyclic antidepressants. *Lancet* **343**, 159–162.

Department of Health (2000). *Prescription Cost Analysis System 1991–1998*. Department of Health: London.

Donoghue, J. M. & Tylee, A. (1996). The treatment of depression: prescribing patterns of antidepressants in primary care in the UK. *British Journal of Psychiatry* **168**, 164–168.

Dunn, R. L., Donoghue, J. M., Ozminkowski, R. J., Stephenson, D. & Hylan, T. R. (1999). Longitudinal patterns of antidepressant prescribing in primary care in the UK: comparison with treatment guidelines. *Journal of Psychopharmacology* **13**, 136–143.

Durkheim, E. (1952). Suicide. *A Study in Sociology* (translation by J. Spalding and G. Simpson). Routledge and Kegan Paul: London.

Freemantle, N., House, A., Song, F., Mason, J. M. & Sheldon, T. A. (1994). Prescribing selective serotonin reuptake inhibitors as strategy for prevention of suicide. *British Medical Journal* **309**, 249–253.

Geddes, J. R., Freemantle, N., Mason, J., Eccles, M. & Boynton, J. (2000). SSRIs versus other antidepressants for depressive disorder. *Cochrane Database of Systematic Reviews* **2**.

Henry, J. A. (1997). Suicide and the cost-effectiveness of antidepressants. *British Journal of Psychiatry* **170**, 88.

Henry, J. A., Alexander, C. A. & Sener, E. K. (1995). Relative mortality from overdose of antidepressants. *British Medical Journal* **310**, 221–224.

Isacsson, G., Holmgren, P., Druid, H. & Bergman, U. (1997). The utilization of antidepressants – a key issue in the prevention of suicide: an analysis of 5281 suicides in Sweden during the period 1992–1994. *Acta Psychiatrica Scandinavica* **96**, 94–100.

Jick, S. S., Dean, A. D. & Jick, H. (1995). Antidepressants and suicide. *British Medical Journal* **310**, 215–218.

Kapur, S., Mieczkowskki, M. & Mann, J. (1992). Antidepressant medications and the relative risk of suicide attempt and suicide. *Journal of American Medical Association* **268**, 3441–3445.

Kelleher, M. J. & Daly, M. (1992). The influence of antidepressants in overdose on the increased suicide rate in Ireland between 1971 and 1988. *British Journal of Psychiatry* **161**, 625–628.

Kelly, S. & Bunting, J. (1998). Trends in suicide in England and Wales, 1982–1996. *Population Trends* **92**, 29–41.

Lewis, G. & Sloggett, A. (1998). Suicide, deprivation, and unemployment: record linkage study. *British Medical Journal* **317**, 1283–1286.

McClure, G. M. G. (2000). Changes in suicide in England and Wales, 1960–1997. *British Journal of Psychiatry* **176**, 64–67.

Meltzer, H., Gill, B. & Petticrew, M. (1995). *OPCS Surveys of Psychiatric Morbidity in Great Britain. Report No. 1. The Prevalence of Psychiatric Morbidity among Adults aged 16–64 Living in Private Households in Great Britain*. HMSO: London.

Milne, S., Alcorn, A. & Bell, A. (1993). Effective and acceptable treatment for depression. *British Medical Journal* **306**, 1126.

Office of Health Economics. (1981). *Suicide and Deliberate Self-Harm*. OHE: London.

Ohberg, A., Vuori, E., Klaukka, T. & Lonnqvist, J. (1998). Antidepressants and suicide mortality. *Journal of Affective Disorder* **50**, 225–233.

Oyefeso, A., Ghodse, H., Clancy, C. & Corkery, J. M. (1999). Suicide among drug addicts in the UK. *British Journal of Psychiatry* **175**, 277–282.

Paykel, E. S., Tylee, A., Wright, A., Priest, R. G., Rix, S. & Hart, D. (1997). The defeat Depression Campaign: psychiatry in the public arena. *American Journal of Psychiatry* **154**, 59–65.

Retterstol, N. (1993). Death due to overdose from antidepressants: experiences from Norway. *Acta Psychiatrica Scandinavica* (suppl. 371), 28–32.

Spina, E., Henthorn, T. K., Eleborg, L., Nordin, C. & Sawe, J. (1985). Desmethylimipramine overdose: nonlinear kinetics in a slow hydroxylator. *Therapeutic Drug Monitoring* **7**, 239–241.

Teicher, M. H., Glod, C. & Cole, J. O. (1990). Emergence of intense suicidal preoccupation during fluoxetine treatment. *American Journal of Psychiatry* **147**, 207–210.

White, C. M., Gailey, R. A., Levin, G. M. & Smith, T. (1997). Seizure resulting from a Venlafaxine overdose. *Annals of Pharmacotherapy* **31**, 178–180.

Whitley, E., Gunnell, D., Dorling, D. & Smith, G. D. (1999). Ecological study of social fragmentation, poverty, and suicide. *British Medical Journal* **319**, 1034–1037.