only be determined by relating treatment to morbidity. Unfortunately, such information is not available, and what information there is on the extent of psychiatric morbidity alone is most unreliable because observer bias, differing parameters, confused nosology and lack of replicability.

To determine some of the reasons for the increased prescribing of psychotropic drugs it is also necessary to examine the sources, diffusion and influence of therapeutic knowledge in order to assess the pressures and demands made upon general practitioners to prescribe these drugs. It is the aim of this report to look at only a few of these problems as follows:

1. To examine national prescribing trends for psychotropic drugs.
2. To report the results of a retrospective study of psychotropic drug prescribing by a group of general practitioners in the Midlands and to examine some of their indications for such therapy.
3. To look at some of the influences affecting drug prescribing in general practice.

1

NATIONAL PRESCRIBING TRENDS OF PSYCHOTROPIC DRUGS

From 1965 to 1970 inclusive there was a 19 per cent increase in the prescribing of psychotropic drugs in England and Wales.* In 1970, 43 per cent of all psychotropic drug prescriptions were for hypnotics, 36 per cent for tranquillizers, 7 per cent for stimulants and appetite suppressants and 14 per cent for antidepressants. Between 1965 and 1970 the prescribing of barbiturate hypnotics decreased by 24 per cent and stimulants and appetite suppressants by 36 per cent. There was an increase in the prescribing of non-barbiturate hypnotics of 145 per cent, a 59 per cent increase in tranquillizer prescribing and an 83 per cent increase in antidepressant drug prescribing. Eighty per cent of all psychotropic drugs prescribed in 1970 were hypno-sedatives or tranquillizers.

TABLE II
PSYCHOTROPIC DRUG PRESCRIBING (ENGLAND AND WALES, 1965–70)

Therapeutic sub-group	*Alterations in number of prescriptions (1965-70)*	*Percentage of all prescriptions for psychotropic drugs (1970)*
	percentage increase or decrease	
Barbiturate hypnotics	*— 24*	*28*
Non-barbiturate hypnotics	*+145*	*15*
Tranquillizers	*+ 59*	*36*
Stimulants and appetite suppressants	*— 36*	*7*
Antidepressants	*+ 83*	*14*
All psychotropic drugs	*+ 19*	*100*

National hypnotic drug prescribing trends

Prescribing of hypnotic drugs increased from 20·1 million prescriptions in 1965 to 20·2 million in 1970. During this period the barbiturate hypnotic drug prescribing rate fell from 17·2 million to 13·1 million whilst non-barbiturate hypnotic drug prescribing increased from 2·9 to 7·1 million. The four most frequently prescribed barbiturate

*The prescribing trends discussed in this chapter are calculated from annual prescribing figures provided by the Department of Health and Social Security.

hypnotic drugs were Soneryl,* Tuinal, Nembutal and Sonalgin (figure 1). Two of these drugs are combined drug preparations; Tuinal contains equal parts of quinalbarbitone and amylobarbitone in 100 mg and 200 mg strengths and Sonalgin contains butobarbitone 60 mg, codeine phosphate 10 mg and phenacetin 225 mg. The rationale of such combinations has often been criticized.

The increase in the prescribing of non-barbiturate hypnotics was almost entirely due to two drugs—Mandrax and Mogadon, both introduced in 1965. By 1970 2·5 million prescriptions for Mandrax were dispensed and 2·6 million prescriptions for Mogadon. These two drugs account for one quarter of all hypnotic drugs prescribed. Mandrax (a non-barbiturate) contains a mixture of methaqualone (250 mg) and diphenhydramine (25 mg). Methaqualone is used as an hypnotic; it can produce dependence† of the barbiturate-alcohol type and potentiate the action of alcohol. It appears to act synergistically with diphenhydramine (an antihistamine) in Mandrax to produce an increased hypnotic effect. Mogadon is a benzodiazepine produced by the makers of the anti-anxiety drugs, Librium and Valium. Its actions are similar to these two drugs but it possesses more marked 'sedative' properties and is presented as a 'sleep-inducer'.

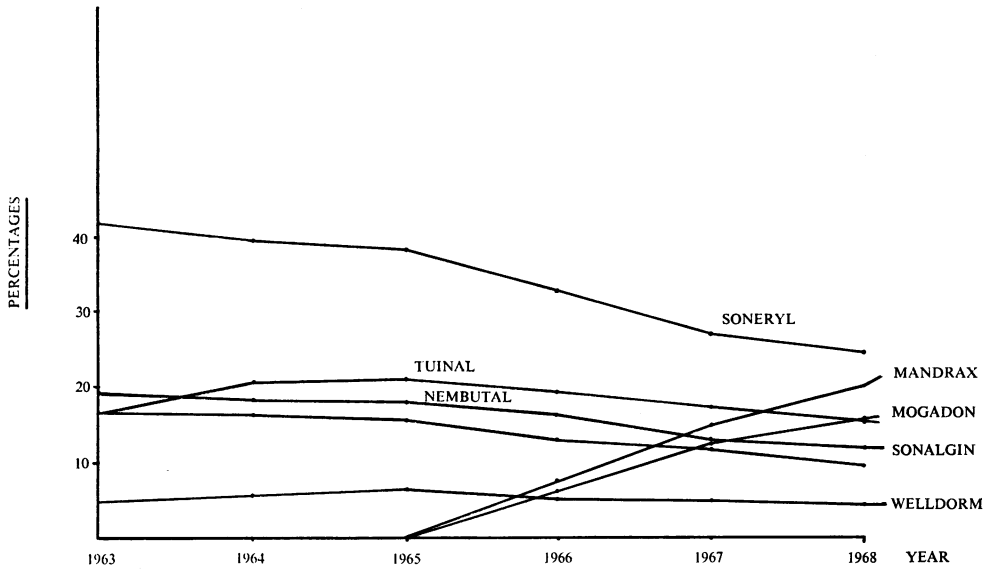

Figure 1
Prescriptions for hypnotic drugs (percentage) (England and Wales, 1963–1968)

It is difficult to interpret the phenomenal increase in the prescribing of Mandrax since it shares most of the disadvantages of the barbiturates and also has the decisive drawback that much less is known about its pharmacology and toxicology. Non-barbiturate hypnotics possess many and diverse chemical and pharmacological properties and therefore, any rational approach to their use requires a thorough knowledge of their actions and effects, particularly in the wake of the thalidamide tragedy. Goodman and Gilman's (1966) summary of the history of glutethimide (*eg*, Doriden) paints a picture typical of many new hypnotics:

> The history of glutethimide is representative of that of many of the new hypnotics. On introduction, it was acclaimed as an effective 'non-barbiturate' hypnotic sedative, free of some of the disadvantages of barbiturates and probably lacking in addiction liability. The drug gained instant and widespread

*The majority of psychotropic drug prescriptions are for proprietary preparations—see Appendix I for list of proprietary and generic names.

†For definition of dependence see Appendix II.

acceptance, and within two years it had become one of the most popular hypnotics in the United States. A prescription survey in 1955 indicated that it was the sixth most frequently prescribed sedative, the first five being barbiturates (cited by McBay and Katsas, 1957). Acute glutethimide intoxication soon became a familiar clinical entity. Sixty-eight cases of glutethimide poisoning, including 14 fatalities, had been described in the medical literature by 1962 (Maher *et al.*, 1962). In the first half of 1962 alone 62 cases of poisoning associated with the ingestion of glutethimide were reported to the Poison Control Center of New York City (Jacobziner and Raybin, 1962). In some instances glutethimide intoxication showed unusual features, making clinical management difficult. Furthermore, by 1962, approximately 20 cases of glutethimide dependence had been reported, in some instances involving frank addiction and severe abstinence phenomena of the type associated with barbiturate withdrawal. Thus, the initial optimism in the pharmacological and clinical literature gave way to more cautious appraisals. Glutethimide is now regarded as a typical general depressant having no especial advantage over the barbiturates, but constituting a satisfactory alternative to the latter if one is needed.

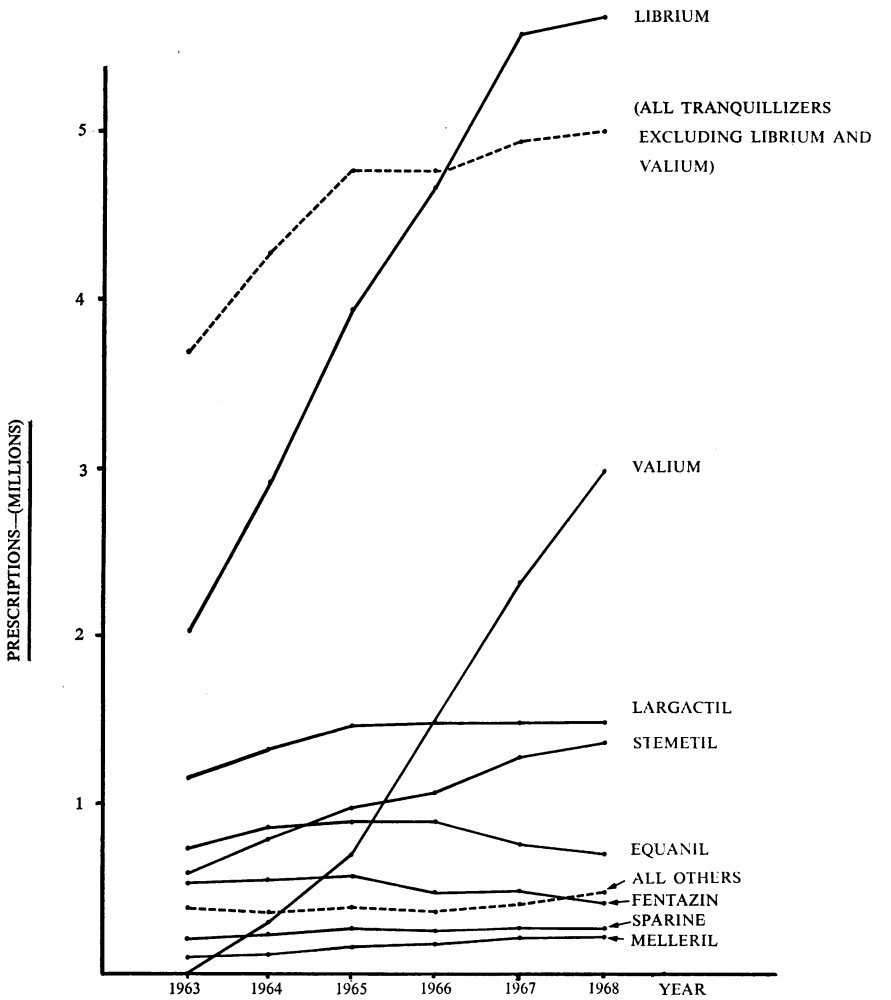

Figure 2
Prescriptions for tranquillizer drugs (excluding hypno-sedatives) (England and Wales, 1963–1968)
Number of prescriptions (millions)

The new hypnotics are all capable of producing dependence of the barbiturate-alcohol type. Over the past decade many of these drugs, particularly Mandrax, have become abused resulting in states of intoxication and dependence. With the exception of Mogadon they are all dangerous when an overdose is taken. The barbiturates still

remain versatile and useful drugs if used selectively and intelligently but the decision to prescribe a barbiturate or non-barbiturate hypno-sedative must obviously lie with the prescriber. It appears, however, that both groups of drugs have certain advantages and certain disadvantages and therefore the indication, rather than the selection of a particular preparation, should determine therapy.

National tranquillizer drug prescribing trends

The prescribing of all tranquillizer drugs (including hypno-sedatives) increased from 10·8 million prescriptions in 1965 to 17·2 million in 1970. This rise was mainly due to a 110 per cent increase in prescribing of the so-called minor tranquillizers (Librium and Valium), whilst the prescribing of the major tranquillizers increased by 49 per cent. During the period 1965 to 1970 the annual prescribing of Librium increased by 1·15 million prescriptions and Valium by 4·1 million prescriptions whilst the minor tranquillizer Equanil showed a decrease (figure 2). The prescribing of Librium increased by 28 per cent and Valium which was introduced in 1963 reached an annual total of 4·7 million prescriptions by 1970 (table III).

Prescriptions for minor and major tranquillizers excluding Librium and Valium showed an increase of 25 per cent between 1965 and 1970, whilst the overall increase in tranquillizer prescribing was 59 per cent (table IV). In 1965 Librium and Valium

TABLE III

PERCENTAGE SHARES OF THE TRANQUILLIZER PRESCRIPTIONS (LIBRIUM, VALIUM AND LARGACTIL) (ENGLAND AND WALES, 1963–1968)

	1963	*1964*	*1965*	*1966*	*1967*	*1968*
Librium (millions)	2·06	2·95	4·00	4·71	5·62	5·74
Percentage of 'minor'	*69·0*	*69·0*	*70·0*	*65·0*	*63·0*	*60·0*
Percentage of all	*35·0*	*39·0*	*42·0*	*43·0*	*43·0*	*41·5*
Valium (millions)	0·057	0·312	0·697	1·48	2·37	3·03
Percentage of 'minor'	*1·7*	*7·0*	*12·0*	*20·5*	*27·0*	*32·0*
Percentage of all	*1·0*	*4·0*	*7·0*	*13·5*	*18·0*	*22·0*
Largactil (millions)	1·16	1·32	1·45	1·49	1·49	1·48
Percentage of 'major'	*41·0*	*40·0*	*39·0*	*40·0*	*37·0*	*35·0*
Percentage of all	*20·0*	*17·5*	*15·2*	*13·6*	*11·5*	*10·7*

TABLE IV

THE PERCENTAGE ANNUAL INCREASE IN PRESCRIBING RATES OF THE 'MAJOR' AND 'MINOR' TRANQUILLIZERS (ENGLAND AND WALES, 1963–1968)

	1963	*1964*	*1965*	*1966*	*1967*	*1968*
Major tranquillizers	—	*16·2*	*13·8*	—	*8·3*	*4·5*
Minor tranquillizers	—	*42·0*	*35·0*	*25·6*	*23·4*	*7·4*
TOTAL	—	*29·5*	*25·6*	*15·5*	*18·3*	*6·5*
Ratio minor and major tranquillizers	1·06	1·29	1·53	1·93	2·2	2·24
Percentages of total for 'minor' ..	*51·5*	*56·4*	*60·5*	*66·0*	*68·8*	*69·3*

accounted for 44 per cent of tranquillizer (excluding hypno-sedatives) prescriptions (figure 3) and by 1970 this had increased to 63 per cent, the number of prescriptions having increased from 4·7 to 9·8 million.

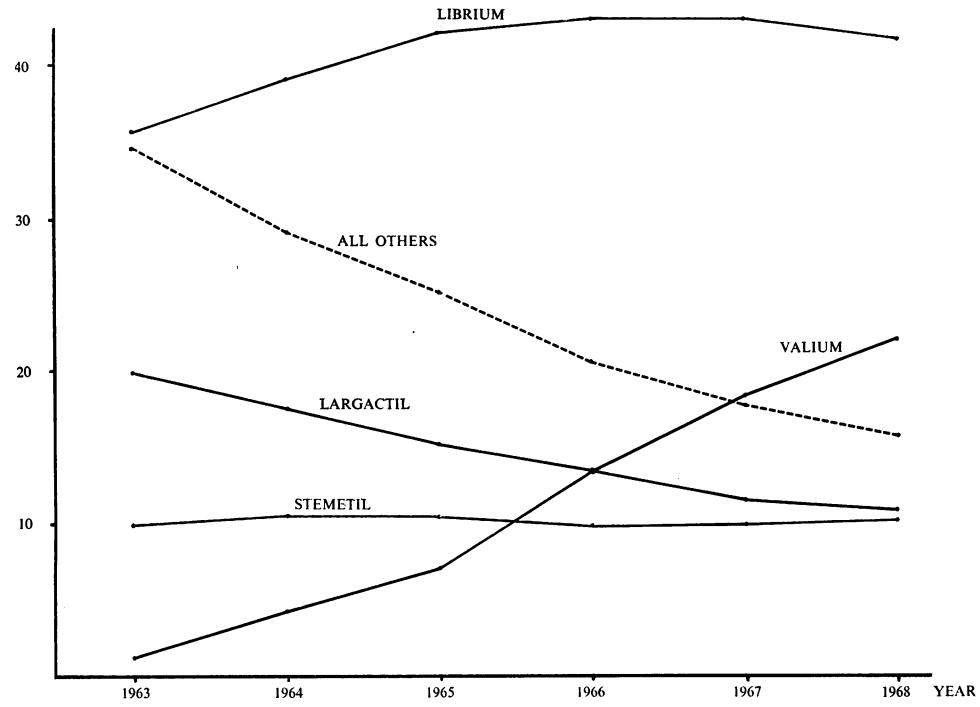

Figure 3
Prescriptions for tranquillizer drugs (percentages) (excluding hypno-sedatives) (England and Wales, 1963–1968)

From 1965 to 1970 inclusive the annual number of prescriptions for phenobarbitone fell from 3·1 million to 2·4 million. Prescriptions for Amytal also fell from 1·67 million to 1·39 million and for Sodium Amytal from 2·09 million to 1·77 million. The prescription rate for meprobamate products (*eg*, Equanil) fell from 0·74 million in 1965 to 0·54 million in 1970. This resulted in an overall fall in annual prescriptions for these products (phenobarbitone, Amytal, Sodium Amytal and meprobamates) of 1·50 million during this period.

The increase in the number of prescriptions dispensed for tranquillizer drugs was due mainly to an increased prescribing of Librium and Valium. These are both benzodiazepines and possess similar pharmacological profiles. It is of interest that when the annual prescribing of one product is rising it is possible to launch a similar product and increase its sales annually; thus the sales of the second product adds to the market of the first rather than replacing it. A third benzodiazepine was launched in 1965 as a sleep inducer (nitrazepam, Mogadon) and these three benzodiazepines, all manufactured by the same firm, are responsible for a major share of hypno-sedative and tranquillizer drug prescribing.

It is difficult to explain the increasing popularity of these drugs in view of the fact that the overall prescribing of the previously popular sedatives (phenobarbitone, Amytal, Sodium Amytal and meprobamate) fell by only 1·50 million prescriptions between 1965 and 1970 compared with the 1·1 million increase in Librium prescriptions and 4·1 million increase in Valium prescriptions during that period. The usefulness of these 'anti-anxiety' drugs or 'minor tranquillizers', remains controversial because of the many

variables in defining anxiety and its response to treatment. They are all central nervous system depressant drugs and categorizing them as minor tranquillizers should not in any way detract from their potential danger of causing such depression and dependency. They are an alternative to the barbiturates and are safer when an overdose is taken, but, as in the case of the non-barbiturate hypnotics, their increased prescribing suggests that factors other than morbidity are influencing their prescribing.

The prescribing of major tranquillizers increased by 49 per cent from 1965 to 1970 whilst the prescribing of minor tranquillizers increased by 220 per cent over the same period. The phenothiazines are the most frequently prescribed major tranquillizers, being widely used in the treatment of schizophrenia and affective disorders such as mania, agitated depression and paranoid disturbances. Most patients with anxiety or neurotic depression tolerate major tranquillizers badly. They may sometimes be useful in the treatment of agitation or confusion in the elderly and in the early stages of depressive disorders when anxiety or agitation are prominent or when there is a history of psychotic behaviour. However, it is again difficult to account for the 49 per cent increase in their use over the period 1965–70, unless they are being used in psychoneurotic disorders which is suggested by the prescribing of the major tranquillizer, Stemetil (prochlorperazine) which is used mainly as symptomatic therapy for vertigo, migraine and nausea. The prescribing of Stemetil (5 mg) tablets increased from 985,000 prescriptions in 1965 to 1,836,000 prescriptions in 1970.

National stimulant and appetite suppressant drug prescribing trends

From 1965 to 1970 the prescribing of stimulant and appetite suppressant drugs decreased by 36 per cent. There was a 24 per cent decrease in prescribing from 1965 to 1968 and a further fall of 13 per cent from 1968 to 1970.

Amphetamines were the most frequently prescribed stimulant and appetite suppressant drugs up to 1966 but since then they have shown a progressive falling off at the rate of 9 per cent per annum, and this is continuing. Between 1966 and 1968 the prescribing of Durophet and Preludin fell, whilst the diethylpropion preparations (Apisate and Tenuate) showed a progressive increase so that by 1968 these products accounted for 46 per cent of all appetite suppressant drug prescriptions. Fenfluramine (Ponderax) introduced in 1965, established itself in 1966 and its prescribing roughly trebled each year so that by 1968 about 36 per cent of all prescriptions for appetite suppressants were for this drug.

Unfortunately, from the time of their introduction the amphetamines were prescribed readily and up to 1968 official support sanctioned their use, despite warnings against the hazards of tolerance, addiction and psychoses (Davidoff and Reifenstine 1937, Monroe and Drell 1947, Connell 1958 and 1968, Johnson and Milner 1966, Scott and Willcox 1963 and Lemere 1966). The capacity of the amphetamines and their derivatives to elevate mood and to induce a state of well-being were obviously the basis for their abuse. Public and professional concern regarding their consumption increased in the late sixties and on 18 March 1968 the Chief Medical Officer of the Ministry of Health wrote to all general practitioners: "It is probable that the bulk of what is now legally used is prescribed for suppression of appetite or the alleviation of depression. A substantial body of authoritative opinion holds that the first of these uses is unnecessary and the second, largely ineffective." The report of the British Medical Association Working Party on amphetamine preparations (November 1968) recommended "that amphetamine and amphetamine-like compounds should only be prescribed for those conditions for which no reasonable alternative exists. These drugs should be avoided as far as possible in the treatment of obesity and their use in the treatment of depression should be avoided."

The transient relief of the symptom of hunger in the management of obesity which is after all a life long problem is of doubtful efficacy yet in 1970 3·4 million prescriptions for these drugs were dispensed. An increasing number of these prescriptions are for

fenfluramine (Ponderax). It is claimed that this drug has a metabolic effect upon obesity by increasing muscle glucose uptake and by enhancing fat mobilization and reducing lipid synthesis. It produces sedation and its success may be related to the decreasing popularity of the stimulant appetite suppressants. However, its success may also be the result of pressures applied to the general practitioner as the result of producer promotion and demands by obese patients who attend for treatment. Since information on diet control is freely available, patients who attend their general practitioner for treatment of their obesity, must expect more, and Yudkin (1967) suggests that they expect the general practitioner to play an active rôle; under these circumstances he may turn to drug therapy.

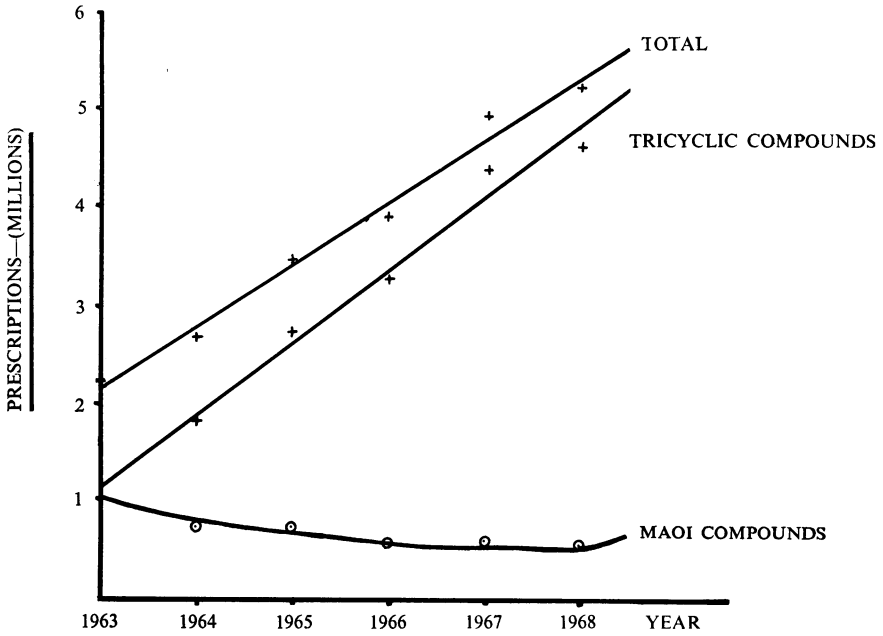

Figure 4
Prescriptions for antidepressant drugs. Number of prescriptions (millions) (England and Wales, 1963–1968)

TABLE V

THE ANNUAL INCREASE IN PRESCRIBING OF TRICYCLIC DRUGS AND THE DECREASE IN PRESCRIBING OF MAO INHIBITOR DRUGS (ENGLAND AND WALES, 1963–1968). (NUMBER OF PRESCRIPTIONS IN MILLIONS)

	1963	*1964*	*1965*	*1966*	*1967*	*1968*
MAO inhibitor drugs	1·079	0·808	0·713	0·575	0·532	0·538
Tricyclic drugs	1·112	1·830	2·721	3·309	4·356	4·690
TOTAL	2·191	2·648	3·434	3·884	4·888	5·228

ANNUAL PERCENTAGE CHANGES IN PRESCRIBING OF TRICYCLIC AND MAO INHIBITOR DRUGS (ENGLAND AND WALES, 1967–1968)

	1963	*1964*	*1965*	*1966*	*1967*	*1968*
MAO inhibitor drugs	—	*— 2·5*	*—11·8*	*—19·4*	*— 7·5*	*+ 1·1*
Tricyclic drugs	—	*+20·6*	*+30·3*	*+13·1*	*+26·0*	*+ 6·7*

National antidepressant drug prescribing trends

Prescriptions for antidepressant drugs increased from 3·5 million prescriptions in 1965 to 6·4 million in 1970. There are two groups of antidepressant drugs—the tricyclic drugs and the monoamine oxidase (MAO) inhibitor drugs and the most noticeable change in their prescribing took place during the period 1963–1968. The prescribing rate of tricyclic drugs increased by 320 per cent (2·19 to 5·23 million) whilst there was a fall of 50 per cent in the prescribing of monoamine oxidase inhibitors (1·079 to 0·538 million (figure 4). In 1963 the ratio of usage of tricyclic drugs to MAO inhibitor drugs was 1·03 and by 1968 this had increased to 8·7 (table V and figure 4).

In 1968 four drugs, Nardil, Parnate, Marplan and Niamid accounted for most of the MAO inhibitor prescriptions. The 320 per cent increase in prescribing of tricyclic drugs was mainly for amitriptyline preparations (mostly Tryptizol) and imipramine preparations (mostly Tofranil) (figures 4 and 5). The prescribing of nortriptyline

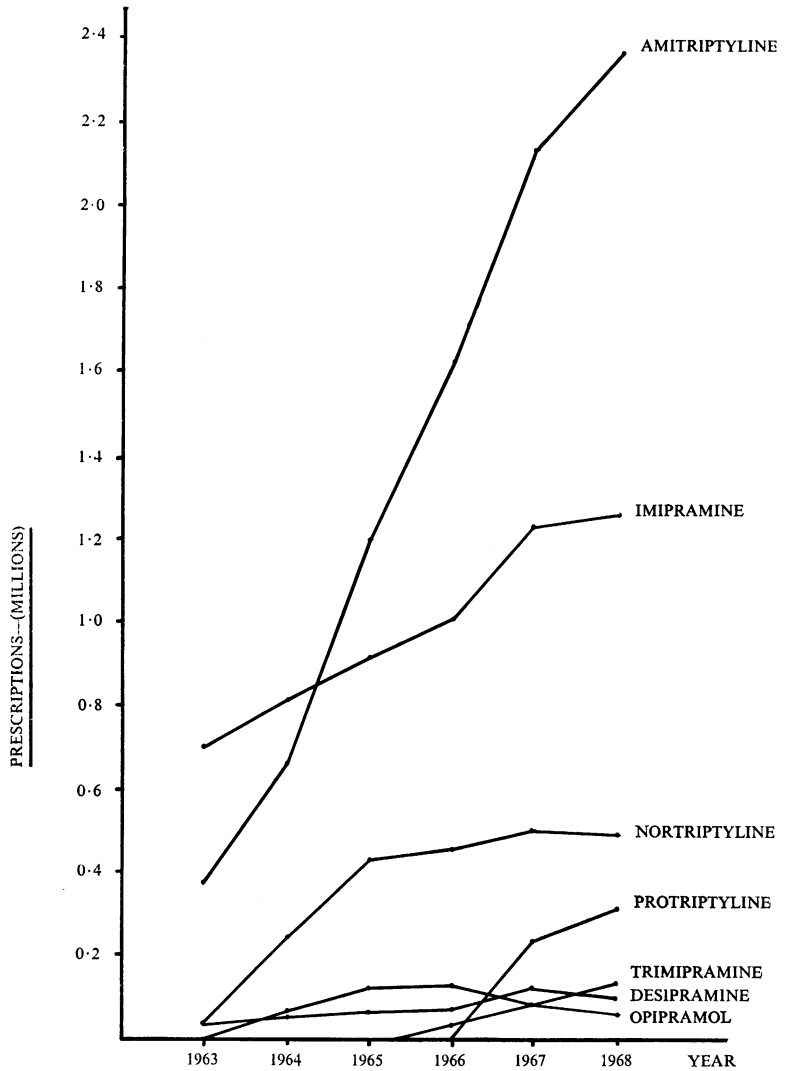

Figure 5
Prescriptions for tricyclic antidepressant drugs. (Number of prescriptions in millions) (England and Wales, 1963–1968)

preparations started to increase rapidly but then levelled off; Aventyl reached about 10 per cent of tricyclic drug prescriptions but only for a short time.

During the past ten years an increasing interest has been shown in the diagnosis and management of depressive disorders, consequent upon the introduction of effective antidepressant drugs and studies of their actions. These drugs have become widely used in both psychiatric and general practice and their popularity is reflected in the increased prescribing of them, from 3·5 million prescriptions in 1965 to 6·4 million in 1970. Clinical trials of antidepressant drugs have produced conflicting results, often due to the current confusion in the recognition of depressive disorders, their classification, their complex presentation and their multi-factorial aetiology.

The tricyclic compounds have established themselves as antidepressant drugs of choice particularly in the treatment of psychotic depressive disorders. The monoamine oxidase inhibitors still have a place in the treatment of atypical depressive and neurotic depressive disorders but have fallen into disrepute because of reported deaths from hypertensive crises caused by food or drug incompatabilities (particularly cheese) and because of reported deaths from hepatitis.

Discussion

During the period 1965–1970 prescriptions for barbiturate hypnotics decreased by 24 per cent and stimulant and appetite suppressants decreased by 36 per cent. Non-barbiturate hypnotic prescriptions increased by 145 per cent, tranquillizers by 59 per cent and antidepressants by 83 per cent. Despite the fall in barbiturate hypnotic drug prescriptions there was an overall increase (0·5 per cent) in hypnotic drug prescribing. This was due to the massive 145 per cent increase in non-barbiturate hypnotics which was accounted for by the prescribing of two non-barbiturates (Mandrax and Mogadon) introduced in 1965. The increase in tranquillizer drug prescriptions was mainly due to an increased prescribing of two drugs (Librium and Valium) and another two drugs (Tryptizol and Tofranil) accounted mainly for the 320 per cent increase in antidepressant drug prescribing. Six drugs (Mandrax, Mogadon, Librium, Valium, Tryptizol and Tofranil) therefore dominated the increase in psychotropic drug prescribing during this period. Further examination of prescribing, showed that the annual increase in prescriptions for psychotropic drugs was 7·5 million from 1965 to 1970. During this period the annual prescribing of four drugs increased by more than 7 million; these were Librium (annual increased prescribing rate 1·1 million), Valium (annual increased prescribing rate 4·1 million), Mogadon (annual increased prescribing rate 2·6 million) and Mandrax (annual increased prescribing rate of 2·5 million).

The increased interest in recognition and treatment of depressive disorders helps to explain the increase in the prescribing of the antidepressant drugs (Tryptizol and Tofranil) but the phenomenal increase in the prescribing of the hypnotics (Mandrax and Mogadon) and the minor tranquillizers (Librium and Valium) is difficult to explain. Could it be that insomnia and anxiety disorders have increased by this amount? Or are patients who attend their general practitioners receiving an increasing amount of drug treatment? A retrospective survey of psychotropic drug prescribing by a group of Midland general practitioners was therefore carried out in order to examine the prescribing patterns of these drugs and some of the indications for their use. These are discussed in the next chapter.