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ORIGINAL REPORT

Did Knowledge, Opinions, Background, and Health Authority Advice Influence Early Prescribing of the Novel Alzheimer's Disease Drug Donepezil in General Practice? — National Postal Survey

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SUMMARY

Background — Donepezil was licensed in the UK in February 1997 for the treatment of Alzheimer's disease.

Aims — To determine the advice from health authorities about prescribing Alzheimer's disease drugs. To determine whether the first general practitioners who prescribed donepezil in England differed from non-prescribers in terms of knowledge, opinions, background, and the prescribing-advice issued by their health authority.

Methods — National postal survey of pharmaceutical advisors. Structured postal survey of all general practitioners in England who prescribed donepezil to two or more patients within the first 6 months of launch, compared with a random sample of non-prescribers.

Results — *Pharmaceutical advisors' survey*: 75/100 pharmaceutical advisors responded, of whom 83% indicated that general practitioners should not initiate prescribing of Alzheimer's disease drugs and 63% said that they should not prescribe, even under shared care arrangements. *General practitioner survey*: 311/473 (66%) prescribers and 484/947 (51%) non-prescribers responded after two mailings. Prescribers were similar to non-prescribers in terms of demographic and practice characteristics, knowledge about Alzheimer's disease, diagnostic and initial management strategies, and the prescribing advice from health authorities. Prescribers were significantly more likely than non-prescribers to strongly agree/agree that new drugs should be prescribed for mild ($p = 0.0008$) and moderate ($p = 0.003$) Alzheimer's disease, that they should normally be initiated ($p = 0.003$) and monitored by a general practitioner ($p < 0.0001$), and that financial constraints should not be a consideration ($p = 0.0001$).

Conclusion — Early prescribers differed from non-prescribers in their opinions about using Alzheimer's disease drugs. Future research should examine methods to promote nationally equitable and rational prescribing of new drugs.

KEY WORDS — general practice; Alzheimer's disease; prescribing; guidelines; prescription-event monitoring

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INTRODUCTION

Several novel agents have recently been marketed for the treatment of chronic diseases, including interferon beta-1b for multiple sclerosis, sildenafil for impotence, leukotriene receptor antagonists for asthma, and donepezil for Alzheimer's disease. New drugs have received increasing attention both in medical journals, fuelled by concerns about whether limited resources are used efficiently,[1–5] and in the media,[6] increasing the likelihood of patients coming forward for treatment.[4,5]

There have been rapid increases in the prescribing of several new drugs without evidence of increases in morbidity,[7–11] raising the question of what factors influence the adoption of new agents. Pharmaceutical company promotion is important in raising awareness, but consultants stimulate general practitioner prescribing.[12] However, heavy marketing does persuade some doctors to start new drugs.[10–14] Qualitative research suggests that reading, professional colleagues and personal experience are important cues to changing prescribing behaviour.[15]

Donepezil was launched in the UK in February 1997 for the symptomatic treatment of mild to moderate Alzheimer's disease.[4] Alzheimer's disease is common in the elderly, carries a large financial cost to the NHS, social services and patients, and impacts substantially on carers.[16] Public expenditure is most expensive in institutional care. Reducing symptoms may reduce the need for community support and delay or prevent patients going into institutional care. Drug expenditure for Alzheimer's disease is low,[16] but new drugs will increase prescribing and shift costs towards primary care.[4] However, donepezil shows only a moderate effect on cognitive function in short term trials, and data on non-cognitive function are limited.[17–21] Recent guidelines advise general practitioners against prescribing donepezil even if initiated by specialists,[22] while others limit prescribing and monitoring to specialists.[23]

We speculated that general practitioners who prescribed donepezil soon after its launch may differ from those who did not. Knowledge of any differences may inform debate about the rational introduction of new drugs. We surveyed all NHS general practitioners in England who had prescribed donepezil to two or more patients within 6 months of its launch, and compared them with a random sample of general practitioners who had not, in terms of knowledge, opinions, background, and the prescribing advice issued by their health authority.

METHOD

Study design

We performed national self-completed structured postal surveys of a sample of general practitioners and of all health authority pharmaceutical advisors in England.

Selection of general practitioners

We accessed the national pharmacovigilance database of the Drug Safety Research Unit, Southampton, which is maintained in collaboration with the Prescription Pricing Authority in England.[24] For selected newly marketed drugs, such as donepezil, details of all NHS dispensed prescriptions are obtained. We identified all ($n = 487$) general practitioners in England who had prescribed donepezil to two or more patients within 6 months of its UK launch ('prescribers'). For each prescriber, two controls doctors from the same health authority, who had not prescribed donepezil within the first 6 months of its launch, and who were not from the same practice as a prescribing doctor, were randomly selected from a database of all general practitioners in England ('non-prescribers'). Random selection was performed using computer generated random numbers assigned to each general practitioner's unique identifier in the database.

General practitioner questionnaire

The general practitioner questionnaire was designed to assess the following in relation to Alzheimer's disease: knowledge, investigations, management options, opinions about diagnosis, management and drug treatment, and background practice and demographic characteristics. Prescribers were asked to identify the original prescriber, plans for follow-up, and self-reported impressions of efficacy and numbers of patients living independently. The questionnaires, together with a covering letter and Freepost envelope, were mailed in February 1998. A second questionnaire, a specific reminder letter, the original covering letter, and a Freepost envelope were sent to all non-respondents in March 1998, with a return date no later than 30 April 1998.

Pharmaceutical advisor questionnaire

A single mail-shot postal survey of all 100 pharmaceutical advisors in England was conducted in January 1998. Pharmaceutical advisors were asked whether or not general practitioners in their health authority area had been advised that they should: (1) not initiate the prescription of licensed Alzheimer's disease drugs on an FP10; (2) not prescribe licensed Alzheimer's disease drugs (even under a shared care arrangement with specialists); (3) make their own decision about prescribing these drugs.

Analysis

Responses from pharmaceutical advisors and general practitioners were linked by means of a unique general practitioner code, containing a number identifying the respective health authority. General practitioner knowledge scores were calculated by assigning one mark for either ticking a correct response or not ticking a false response. Prescribers were compared with non-prescribers using CLINSTAT software to compute the χ^2 statistic with Yates' correction for two by two tables, the χ^2 test for trend for ordered variables, and the comparison of a sample mean with a sample mean.[25] The median number of partners in the prescribing group was compared with non-prescribers using the two-sample Wilcoxon rank sum test performed using STATA software.[26] Post-hoc estimates of study power were computed on STATA.[26] The number of general practitioner responses was large enough to detect important differences in the variables. For example, the power to detect a significant difference ($p < 0.05$) in mean knowledge scores of 0.5 (out of 17) was 96.2%.

PHARMACEUTICAL ADVISOR SURVEY RESULTS

Overall, 75% (75/100) of pharmaceutical advisors responded after one mailing.

Initiation of prescription

Of those who responded, 83% indicated that general practitioners in their area had been advised not to initiate an FP10 prescription for any licensed drug for Alzheimer's disease. There were no reports of general practitioners being advised that they could initiate such a prescription.

Shared care prescription

Of those who responded, 63% indicated that general practitioners had been advised that they should not prescribe licensed Alzheimer's disease drugs (even under a shared care arrangement with the specialist). A total of 16% indicated that such advice had not been given.

Own decision

Only 7% of responders indicated that general practitioners could make their own decision about prescribing these drugs, and 43% responded that they should not. The remainder had already completed one of the other sections.

GENERAL PRACTITIONER SURVEY RESULTS

Response rates

487 general practitioners had prescribed donepezil to two or more patients within the first 6 months of its launch, of which 5 had previously indicated that they did not wish to take part in our studies. We therefore mailed 482 prescribers (99%). A total of 974 randomly selected non-prescribers were identified, of which all were mailed. After one mailing, 227 (47%) prescribers and 372 (38%) non-prescribers had returned completed questionnaires. After two mailings, a total of 311 (65%) prescribers had returned completed questionnaires, and 62 prescribers had returned uncompleted questionnaires. Of the 62 uncompleted questionnaires, 9 doctors were either on sick leave, had moved, had retired or were on maternity leave and could not complete the questionnaire. The final response rate for prescribers was therefore 66% (311/473). After the second mailing, a total of 484 (50%) non-prescribers had returned completed questionnaires, and 160 had returned uncompleted questionnaires. Of the 160 uncompleted questionnaires, 27 doctors were unavailable to complete the survey due to absence. The final response rate for non-prescribers was therefore 51% (484/947).

Table 1 — Demographic and practice characteristics of responders

	Prescriber ($n = 311$)	Non-prescriber ($n = 484$)	p value
Mean age in years (SD)	45.6 (8.2)	45.3 (8.4)	0.6
No. of females (%)	54 (17.4)	118 (24.3)	–
No. of males (%)	251 (80.7)	359 (74.0)	0.02[a]
Mean years since qualification (SD)	21.6 (8.8)	21.2 (8.9)	0.5
Mean years in general practice (SD)	15.2 (7.5)	14.4 (7.9)	0.2
Rural (No., %)	54 (17.5)	70 (14.5)	–
Urban (No., %)	102 (33.0)	200 (41.3)	–
Suburban (No., %)	72 (23.3)	103 (21.3)	–
Semi-rural (No., %)	72 (23.3)	101 (20.9)	0.2[b]
Training practice (No., %)	107 (34.4)	135 (27.9)	0.046
Median partnership size (interquartile range)	5 (1,5)	3 (2,5)	0.0002[c]
Mean list size per partner (SD)	2029.3 (1297.0)	1995.6 (918.3)	0.7
Receive deprivation allowance (No., %)	81 (26.0)	147 (30.4)	0.2
Fundholding (No., %)	143 (46.0)	233 (48.1)	0.7
Geriatric/psychogeriatric outreach clinic (No., %)	13 (4.2)	15 (3.1)	0.4
Community psychiatric nurse (No., %)	117 (37.6)	203 (41.9)	0.2
Physical therapy (No., %)	122 (39.2)	171 (35.3)	0.2

[a]χ^2 with 1 degree of freedom. [b]Overall χ^2 with 3 degrees of freedom. [c]Two-sample Wilcoxon rank-sum (Mann–Whitney) test.

Non-responders

Data on health authority advice and prescribing status were available for non-responders. There were no differences in reported health authority advice when either prescribing responders were compared with prescribing non-responders or when non-prescribing responders were compared with non-prescribing non-responders.

Health authority advice by prescribing status

Overall, 58% of prescribers and 57% of non-prescribers were from a health authority that had advised against general practitioners initiating prescribing for Alzheimer's disease drugs. 37% of both prescribers and non-prescribers were from a health authority that had advised against prescribing even under shared-care arrangements. Only 4% and 6% of prescribers and non-prescribers respectively were in health authorities where they had been advised that they could make their own prescribing decisions.

Demographic and practice characteristics of responders

Prescribers were significantly more likely to be male, from training practices, and from practices with a higher median partnership size (Table 1). There was no difference by urban, rural, suburban or semi-rural location ($p = 0.1$). The proportion of males (74%) in our non-prescribing group was similar to the national distribution of general practitioner principals (18 926/26 948; 70%).[27] The mean patient list size amongst the non-prescribing group of doctors (1996) was similar to the mean list size of principals in England (1881), as was the mean partnership size (3.4 versus 3.0 respectively).[27] The proportion of fundholding practices in both groups was similar to the 47% in England in April 1997 (4238/9004, NHS Executive — personal communication). The proportion of training practices at 28% in our control group was low, when compared with 3277 trainers available for 9004 practices in England (36%).[27]

Knowledge, investigations and management

There was little difference between prescribers and non-prescribers in terms of knowledge scores, routine investigations and early management strategies (Table 2). Symptoms and signs which were most often ticked by prescribers and non-prescribers as indicating the presence of Alzheimer's disease were: memory loss (97%–99% respectively); learning difficulty (86%–85%); behaviour change (85%–88%); diminished judgement (79%–82%); and absence of alternative causes of dementia (77%–78%). Overall, 55% of responders ticked agitation, apathy and withdrawal, and loss

Table 2 — Knowledge scores, investigations and management of patients when Alzheimer' disease is *first* suspected

	Prescribed donepezil $n = 311$	Non prescribed donepezil $n = 484$	p value[a]
Mean knowledge score (SD)	12.3 (1.8)	12.3 (1.9)	0.6
Investigations undertaken			
Serum electrolytes, liver function, and erythrocyte sedimentation tests (No., %)	267 (85.9)	424 (87.6)	0.6
Serum thyroid function test (No., %)	288 (92.6)	451 (93.2)	1
Serum B12 test (No., %)	175 (56.3)	308 (63.6)	0.05
Serum syphillis screen (No., %)	104 (33.5)	194 (40.1)	0.08
Blood glucose test (No., %)	221 (71.1)	348 (71.9)	0.9
Urinalysis	201 (64.6)	328 (67.8)	0.4
Chest x-ray (No., %)	106 (34.2)	195 (40.3)	0.1
Computed tomography (CT) scan (No., %)	38 (12.2)	53 (11.0)	0.7
Cognitive function tests (No., %)	195 (62.7)	291 (60.1)	0.5
Early management			
Refer to a hospital consultant (No., %)	118 (38.1)	217 (44.8)	0.08
Wait and see (No., %)	174 (56.1)	241 (49.8)	0.08
Prescribes a drug (No., %)	8 (2.6)	9 (1.9)	0.5
Discuss concerns with patient (No., %)	81 (26.2)	97 (20.0)	0.047
Discuss concerns with carer/spouse (No., %)	221 (71.3)	329 (68.1)	0.3

SD = standard deviation. [a]Knowledge scores compared using t-test; investigations undertaken and early management compared using χ^2 (1 degree of freedom) with Yates' correction.

of interest. The following cognitive disturbances were less often ticked as indicating Alzheimer's disease by prescribers and non-prescribers: aphasia (language disturbance) (36%); apraxia (impaired ability to carry out motor activities) (16%); agnosia (failure to recognise or identify objects) (23%–17%). Non-prescribers were more likely to undertake serum B12 tests ($p = 0.05$) and were less likely to discuss their concerns with patients ($p = 0.047$) when they first suspected the presence of Alzheimer's disease.

Opinions about the diagnosis and management of Alzheimer's disease

There were no differences between responding prescribers and non-prescribers in response to various statements about the diagnosis and management of Alzheimer's disease (Table 3). Over 80% of prescribers and non-prescribers agreed/strongly agreed that mini-mental state exam in general practice is necessary to assess patients with impaired cognitive function and that in the care of Alzheimer's disease patients, their main role is not to medicate but to provide support. 57% of prescribers and 51% of non-prescribers agreed/strongly agreed they are responsible for diagnosing Alzheimer's disease and ruling out other forms of dementia, and 59%–65% respectively agreed/strongly agreed that referral to a specialist is necessary for most patients with mild to moderate Alzheimer's disease. Of those doctors who answered this question, 30% (88/296) of prescribers and 25% (114/456) of non-prescribers ($p = 0.2$) both agreed/strongly agreed that general practitioners were responsible for diagnosis *and* disagreed/strongly disagreed that specialist referral was necessary for mild to moderate Alzheimer's disease. On the other hand, 33% (97/296) of prescribers and 40% (181/456) of non-prescribers ($p = 0.07$) both disagreed/strongly disagreed that general practitioners were responsible for diagnosis *and* agreed/strongly agreed that specialist referral was necessary for mild to moderate Alzheimer's disease.

Opinions about the drug treatment of Alzheimer's disease (Table 4)

Prescribers were significantly more likely than non-prescribers to strongly agree/agree that these new drugs should be prescribed with *mild* (40% versus 26% respectively; $p = 0.0008$) and *moderate* Alzheimer's disease (48% versus 34% respectively; $p = 0.003$); that new drugs for Alzheimer's disease should normally be initiated by a general

Table 3 — Opinions about the diagnosis and management of Alzheimer' disease amongst responding prescribers ($n = 311$) and non-prescribers ($n = 484$)

Statement		Strongly agree	Agree	Disagree	Strongly disagree	p value[a]
GPs are responsible for diagnosing Alzheimer's disease and ruling out other forms of dementia	Prescribers (%)	13 (4.2)	165 (53.1)	104 (33.4)	20 (6.4)	
	Non-prescribers (%)	17 (3.5)	229 (47.3)	188 (38.8)	32 (6.6)	0.09
Mini-mental state exam in general practice is necessary to access patients with impaired cognitive function	Prescribers (%)	44 (14.1)	222 (71.4)	30 (9.6)	4 (1.3)	
	Non-prescribers (%)	57 (11.8)	358 (74.0)	43 (8.9)	5 (1.0)	0.3
In the care of Alzheimer's disease patients, the main role for GPs is not to medicate but support	Prescribers (%)	52 (16.7)	202 (65.0)	40 (12.9)	5 (1.6)	
	Non-prescribers (%)	79 (16.3)	340 (70.2)	45 (9.3)	4 (0.8)	0.5
Referral to a specialist is necessary for most patients with mild to moderate Alzheimer's disease	Prescribers (%)	33 (10.6)	151 (48.6)	107 (34.4)	9 (2.9)	
	Non-prescribers (%)	58 (12.0)	257 (53.1)	138 (28.5)	14 (2.9)	0.3

Missing and don't know responses not included.
[a]χ^2 test for trend (1df).

practitioner (14% versus 6% respectively; $p = 0.003$); that patients prescribed drugs for Alzheimer's disease should be monitored by a general practitioner (42% versus 21% respectively; $p < 0.0001$); and that financial constraints should not be a consideration in determining which patients are prescribed Alzheimer's disease specific drugs (55% versus 38% respectively; $p = 0.0001$). Most general practitioners thought that carers should be consulted when determining the effectiveness of the drug treatment (94% and 89%). Responders were divided over whether drugs should normally be discontinued for lack of efficacy on the advice of a specialist (46%–49% agreed/strongly agreed; 46%–31% disagreed/strongly disagreed).

Information about 445 patients prescribed donepezil

A total of 253 prescribers answered further questions about the prescribing of donepezil to 445 individual patients (Table 5). Most patients were originally prescribed the drug by a specialist (66%). In 39% of cases responding doctors stated that they had originally prescribed the drug on an FP10. Private prescribing was infrequent (3% of cases). Responding prescribers felt that 40% of the 445 patients had improved, 13% had declined, and 40% had noted no change. Only 31% of these 445 patients prescribed donepezil were living independently. Doctors were divided in their plans for follow-up: responders stated that the plan was for regular assessment by the general practitioner for 34% of patients, and regular assessment by a specialist for 40%. The remaining doctors did not respond (24%), or had no specific plans (3%).

DISCUSSION

There was only a moderate response rate to the general practitioner survey of non-prescribers (51%) compared with prescribers (66%). However, the proportions of responders and non-responders were similar by health authority advice, and responding non-prescribers were similar to the distribution of general practitioners in England by gender, mean list size, mean partnership size,[27] and fundholding status. The proportion of training practices was broadly similar to national statistics on the number of trainers (assuming some practices have more than one trainer). These data argue against significant response bias by the control group.

Prescribers were similar to non-prescribers in their demography, practice characteristics, knowledge scores, diagnostic and management strategies, and health authority advice. A greater proportion of early prescribers compared with non-prescribers reported that they were willing to prescribe for mild and moderate Alzheimer's disease, for which

Table 4 — Opinions about the drug treatment of Alzheimer' disease amongst responding prescribers ($n = 311$) and non-prescribers ($n = 484$)

Statement		Strongly agree	Agree	Disagree	Strongly disagree	p value[a]
These new drugs should be prescribed for patients with mild Alzheimer's disease	Prescribers (%)	15 (4.8)	108 (34.7)	94 (30.2)	23 (7.4)	
	Non-prescribers (%)	16 (3.3)	110 (22.7)	155 (32.0)	61 (12.6)	0.0008
These new drugs should be prescribed for patients with moderate Alzheimer' disease	Prescribers (%)	11 (3.5)	139 (44.7)	61 (19.6)	18 (5.8)	
	Non-prescribers (%)	7 (1.4)	159 (32.9)	117 (24.2)	39 (8.1)	0.003
These new drugs should be prescribed for patients with severe Alzheimer's disease	Prescribers (%)	6 (1.9)	41 (13.2)	130 (41.8)	57 (18.3)	
	Non-prescribers (%)	10 (2.1)	79 (16.3)	154 (31.8)	96 (19.8)	0.6
These new drugs for Alzheimer's disease should normally be initiated by a GP	Prescribers (%)	2 (0.6)	41 (13.2)	128 (41.2)	114 (36.7)	
	Non-prescribers (%)	3 (0.6)	25 (5.2)	187 (38.6)	224 (46.3)	0.003
Patients prescribed these new drugs for Alzheimer's disease should be monitored by a GP	Prescribers (%)	2 (0.6)	128 (41.2)	112 (36.0)	45 (14.5)	
	Non-prescribers (%)	6 (1.2)	95 (19.6)	201 (41.5)	124 (25.6)	<0.0001
Drugs for Alzheimer' disease should normally only be discontinued for lack of efficacy on the advice from a specialist	Prescribers (%)	9 (2.9)	133 (42.8)	114 (36.7)	29 (9.3)	
	Non-prescribers (%)	28 (5.8)	209 (43.2)	120 (24.8)	36 (7.4)	0.4
Carers should almost always be consulted when determining the effectiveness of an Alzheimer' disease drug treatment	Prescribers (%)	91 (29.3)	200 (64.3)	4 (1.3)	3 (1.0)	
	Non-prescribers (%)	119 (24.6)	312 (64.5)	10 (2.1)	3 (0.6)	0.2
Financial constraints should not be a consideration in determining which patients are prescribed Alzheimer's disease specific drugs	Prescribers (%)	43 (13.8)	128 (41.2)	90 (28.9)	26 (8.4)	
	Non-prescribers (%)	35 (7.2)	148 (30.6)	181 (37.4)	61 (12.6)	0.0001

Missing and don't know responses not included.
[a]χ^2 test for trend (1df).

donepezil is currently licensed,[28] and to monitor patients (Table 4). Some (15%–18%) doctors would prescribe for severe disease, although there are no efficacy data supporting such prescribing. Some of both prescribers (14%) and non-prescribers (6%) would initiate treatment, countermanding the Standing Medical Advisory Committee (SMAC) recommendation that only specialists initiate and monitor donepezil.[23] SMAC supports general practitioner prescribing only as part of a shared care protocol. However, in agreement with many general practitioners in our study, some authors do not advocate routine specialist referral.[29,30] Our prescribers were less likely than non-prescribers to consider financial constraints. These issues would probably be best resolved by the development at local level of methodologically valid guidelines.[31]

Despite advice from Health Authorities and subsequent SMAC guidelines, prescribing of donepezil to individual patients was often initiated by general practitioners (173/445; 39%) (Table 5). Although specialist monitoring is recommended,[23] only 40% of patients prescribed donepezil were being actively followed up by a specialist. These results are subject to recall bias, but given that the numbers of patients were small and any prescribing would be a significant event, this bias is likely to be minimal.

The majority of health authority prescribing advisors indicated that general practitioners should resist or restrict use of donepezil. However, an

Table 5 — Information about 445 patients prescribed donepezil by 253 responding prescribers

Question	No. of patients (%) $n = 445$
How many patients were originally prescribed the drug by[a]:	
A specialist?	294 (66.1)
You on an FP10?	173 (38.9)
Privately?	13 (2.9)
How many of these patients do you consider:	
Improved?	178 (40.0)
Declined?	58 (13.0)
No change?	177 (39.8)
Don't know	32 (7.2)
How many of these patients are living independently?	136 (30.6)
What plans do you have for monitoring these patients?	
No specific plans	11 (2.5)
Regular assessment by GP	149 (33.5)
Regular assessment by specialist	177 (39.8)
No response	108 (24.3)

[a]Numbers are greater than total number of patients because some doctors responded more than once.

equal proportion of early donepezil prescribers (58%) and non-prescribers (57%) were advised not to initiate donepezil, or were advised against prescribing them even under shared-care arrangements (37% and 37%). Prescribers may have been influenced by promotional literature or pressure form anxious patients and carers.[12,13,32] Some early prescribers may have been influenced by the credibility resulting from specialist prescribing. Early adopters of innovations are swayed by written information, scientific arguments and credible sources, while later adopters are generally considered to be more traditional and driven by laws.[33]

Early prescribers were more likely than non-prescribers to be male, from a training practice, and from practices with more partners (Table 1), although the numerical differences were small. We did not replicate the findings of an earlier study which found that the mean list sizes of early prescribers of new drugs were larger than for a sample of late prescribers.[12]

Most general practitioners are confident about making the diagnosis of dementia.[34] Our results suggest that the core diagnostic criteria used by general practitioners were memory loss, learning difficulty, behaviour change, diminished judgement, and absence of alternative causes of dementia. However, several important cognitive disturbances (aphasia, apraxia, and agnosia) were not generally recognised as indicating Alzheimer's disease.

When investigating patients with dementia, primary care guidelines recommend that general practitioners use formal cognitive testing to enhance clinical judgement.[22] We found that the majority (60%) of prescribers and non-prescribers reported using cognitive function tests routinely (Table 2). The guidelines also stress that general practitioners should be aware of reversible causes of dementia. The vast majority of our responders ($>85\%$) performed erythrocyte sedimentation rate, biochemistry, and thyroid function tests as recommended.[22] Fewer responders performed urinalysis (65%–68%).

When Alzheimer's disease was first suspected, 26% of prescribers and 20% of non-prescribers would discuss their concerns with the patient (Table 2). Previous reports suggest that 39% of general practitioners and 44% of psychiatrists inform patients with Alzheimer's disease of their diagnosis.[34,35] We asked about when the disease was first suspected, when general practitioners may be even more reluctant to disclose their concerns because of diagnostic uncertainty.[34] However, we found that between 71% and 68% of responders would discuss their concerns with the carer or spouse at this stage, a paradox which raises important ethical issues.

In line with guidelines, most responders ($>80\%$) favoured formal mini-mental state examination in general practice, and agreed that their role was mainly to provide support[22,23] (Table 3). However, prescribers and non-prescribers were equally split about who should diagnose Alzheimer's disease, and whether or not referral to a specialist was necessary for mild to moderate Alzheimer's disease.

CONCLUSION

The paper provides evidence that although general practitioner knowledge about Alzheimer's disease and its diagnosis is good, the new drug donepezil is not being prescribed equitably. There is some evidence of departure from published guidelines. Future research should determine the best method of promoting equitable, high quality and cost effective prescribing of newly launched drugs,

KEY POINTS

- After the launch of donepezil for Alzheimer's disease in February 1997, most health authority prescribing advisors in England advised that general practitioners should resist or restrict its use
- 58% of general practitioners who prescribed donepezil soon after its launch had been advised by their health authority not to initiate a prescription for donepezil, and 37% had been advised against prescribing donepezil even under shared-care arrangements
- Early prescribers of donepezil were similar to non-prescribers in terms of their demography, practice characteristics, and health authority advice. Both groups had a good level of knowledge about diagnosis and management of Alzheimer's disease
- Over 50% of both prescribers and non-prescribers felt that general practitioners were responsible for the diagnosis of Alzheimer's disease, and over 80% felt that the mini-mental state exam was a necessary part of the assessment
- Early prescribers were more likely than non-prescribers to agree that donepezil should be prescribed for mild to moderate Alzheimer's disease, that donepezil should normally be initiated and monitored by a general practitioner, and that financial constraints should not be a consideration

such as donepezil. This research should recognise that in common conditions, like Alzheimer's disease, most prescribing occurs in primary care.

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REFERENCES

1. Ferner, R. E. Newly licensed drugs. *Br. Med. J.* 1996; **313**: 1157–1158.
2. Freemantle, N., Henry, D., Maynard, A. and Torrance, G. Promoting cost effective prescribing. *Br. Med. J.* 1995; **310**: 955–956.
3. Bradley, C. How to evaluate a new drug in general practice. *Prescribers J.* 1997; **37**: 158–165.
4. Kelly, C. A., Harvey, R. J. and Cayton, H. Drug treatments for Alzheimer's disease. *Br. Med. J.* 1997; **314**: 693–694.
5. Smith, R. Viagra and rationing. *Br. Med. J.* 1998; **317**: 760–761.
6. Jones, G. Costly NHS drugs may be rationed. *Daily Telegraph* 22 October:1, 1997.
7. Martin, R. M., Lim, A. G., Kerry, S. M. and Hilton, S. R. Trends in prescribing H_2-receptor antagonists and proton pump inhibitors in primary care. *Aliment. Pharmacol. Therap.* 1998; **12**: 797–805.
8. Martin, R. M., Hilton, S. R., Kerry, S. M. and Richards, N. M. General practitioners' perceptions of the tolerability of antidepressant drugs: a comparison of selective serotonin reuptake inhibitors and tricyclic antidepressants. *Br. Med. J.* 1997; **314**: 646–651.
9. Martin, R. M., Kerry, S. M. and Hilton, S. R. Initial treatment choices, second line therapy and reasons for stopping medication in the treatment of hypertension in general practice: 1990–1995. *Pharmacoepidemiol. Drug Safe.* 1997; **6**: 253–261.
10. McGavock, H., Webb, C. H., Johnston, G. D. and Milligan, E. Market penetration of new drugs in one United Kingdom region: implications for general practitioners and administrators. *Br. Med. J.* 1993; **307**: 1118–1120.

11. Davey, P. G., Bax, R. P., Newey, J., Reeves, D., Rutherford, D. and Slack, R *et al*. Growth in the use of antibiotics in the community in England and Scotland in 1980–93. *Br. Med. J.* 1980; **312**: 613.
12. Bradley, C. P. Decision making and prescribing patterns — a literature review. *Family Pract*. 1991; **8**: 276–287.
13. Taylor, R. J. and Bond, C. M. Change in established prescribing habits of general practitioners: an analysis of initial prescriptions in general practice. *Br. J. Gen. Pract*. 1991; **41**: 244–248.
14. Inman, W. and Pearce, G. Prescriber profile and post-marketing surveillance. *Lancet* 1993; **342**: 658–661.
15. Armstrong, D., Reyburn, H. and Jones, R. A study of general practitioners' reasons for changing their prescribing behaviour. *Br. Med. J.* 1996; **312**: 949–952.
16. Alzheimer's Disease in the UK: Burden of disease and future care. *Health Policy Review Paper* no 12, Imperial College of Science, Technology and Medicine, University of London, 1998.
17. Rogers S. L., Friedhoff, L. T. and Donepezil Study Group. The efficacy and safety of donepezil in patients with Alzheimer's disease: results of US multicentre randomised, double blind, placebo-controlled trial. *Dementia* 1996; **7**: 293–303.
18. Rogers, S. L., Doody, R. S., Mohs R. C., Friedhoff, L. T. and Donepezil Study Group. Donepezil improves cognition and global function in Alzheimer' disease. A 15 week, double blind, placebo controlled study. *Arch. Intern. Med.* 1998; **158**: 1021–1031.
19. Stein, K. Donepezil in the treatment of mild to moderate dementia of the Alzheimer's type (SDAT). *Report to the South and West Development and Evaluation Committee (DEC)* number 69, Bristol, NHS Executive, June, 1997.
20. Rogers, S. L., Farlow, M. R., Doody, R. S., Mohs, R. C. and Friedhoff, L. T. A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Alzheimer' disease. *Neurology* 1998; **50**: 136–145.
21. Anon. Donepezil Update. *Drug Therapeut. Bull.* 1998; **36**: 60–61.
22. Eccles, E., Clarke, J., Livingstone, M., Freemantle, N. and Mason, J. for the North of England Evidence Based Dementia Guideline Development Group. *Br. Med. J.* 1998; **317**: 802–808.
23. Standing Medical Advisory Committee (SMAC). *The Use of Donepezil for Alzheimer's Disease*. UK: Department of Health, April, 1998.
24. Mann, R. D. Prescription-event monitoring — recent progress and future horizons. *Br. J. Clin. Pharmacol*. 1998; **46**: 195–201.
25. Bland, M. CLINSTAT. London: St. George's Hospital Medical School, 1994.
26. StataCorporation. STATA *Statistical Software*: Release 5.0 TX (Texas). College Station, 1997.
27. Department of Health. *General Medical Services Basic Statistics, England and Wales*. Leeds: Department of Health, NHS Executive, 1997.
28. Eisai Europe Ltd. *Aricept*. Summary of Product Characteristics. London: Commonwealth House, 1997.
29. Lovestone, S., Graham, N. and Howard, R. Guidelines on drug treatments for Alzheimer's disease. *Lancet* 1997; **350**: 232–233.
30. Mackay, A. V. P. Issues in drug treatments for Alzheimer's disease. *Lancet* 1997; **350**: 887.
31. Eccles, E., Clapp, Z., Grimshaw, J., Adams, P. C., Higgins, B., Purves, I. and Russell, I. North of England evidence based guidelines development project: methods of guideline development. *Br. Med. J.* 1996; **312**: 760–762.
32. Melzer, D. New drug treatment for Alzheimer' disease: lessons for healthcare policy. *Br. Med. J.* 1998; **316**: 762–764.
33. Grol, R. Implementing guidelines in general practice. *Quality in Health Care* 1992; **1**: 184–191.
34. Vassilas, C. A. and Donaldson, J. Telling the truth: what do general practitioners say to patients with dementia or terminal cancer? *Br. J. Gen. Pract*. 1998; **48**: 1081–1082.
35. Clafferty, R. A., Brown, K. W. and McCabe, E. Under half of psychiatrists tell patients their diagnosis of Alzheimer' disease. *Br. Med. J.* 1998; **317**: 603.

