Cost-effectiveness of clozapine†

A UK clinic-based study

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Background Schizophrenia is highly expensive in calculable and incalculable costs. Measures which impact the cost in the most severely affected are likely to produce the greatest cost reductions. Studies regarding clozapine in the USA have demonstrated clear cost-effectiveness, despite the high prescription costs. There are no prior UK studies.

Method We performed a cost-effectiveness analysis comparing the three years prior to commencing clozapine to the period following establishment of clozapine treatment (mean 36.4 months) for 26 patients with chronic schizophrenia or schizoaffective disorder.

Results There was a significant improvement in all clinical ratings applied (and a mean net saving of £3768 per annum). The cost-effectiveness of clozapine was double that of conventional neuroleptics (15.2 pre-, 33.0 post-clozapine, $P<0.005$).

Conclusions As a naturalistic study our data provide valuable information on the cost-effectiveness of clozapine in the UK. Our methodology could be applied in a community setting or in the study of another atypical neuroleptic.

With an annual treated prevalence estimated as 185 400 and an average annual direct cost of £2138 per case, the treatment of schizophrenia has been estimated as requiring at least £396 million, or 1.6% of the total UK health care budget, with an indirect cost to society of £1.7 billion secondary to lost production by those affected (Davies & Drummond, 1994). Measurement of the in-patient expenditure of the NHS (Department of Health, 1996) gives an even higher value for the percentage of expenditure incurred by the treatment of schizophrenia (5.4%), with learning disability, stroke and schizophrenia together accounting for over one-fifth of total in-patient expenditure.

The above cost estimate does not include the figures secondary to loss of earnings by carers; in a survey of 120 patients, Johnstone *et al* (1991) found that in 2.5% of cases a family member had ceased work to become a carer. Furthermore, the most difficult to quantify in economic terms, but arguably the most significant component of the cost of schizophrenia to society, is the cost of pain and suffering to those with schizophrenia, their families, and the wider community, including that incurred secondary to premature mortality.

The mortality in schizophrenia is approximately twice that in the general population, with the risk of suicide being at least 10 times higher (Allebeck, 1989; Anderson *et al*, 1991). Similarly, a particularly costly, although rare outcome in schizophrenia is homicide. During a 12-month period prior to March 1995 there were a total of 39 homicides in England committed by those with a mental illness, of whom 16 had schizophrenia (Royal College of Psychiatrists, 1996).

Using Prudo & Blum's (1987) classification of schizophrenia into five different outcome groups, Davies & Drummond (1994) have provided estimates of the lifetime direct costs per outcome group. These demonstrate that 97% of the cost is incurred by the two most severely affected outcome groups, who comprise less than 50% of a one-year incidence cohort.

Clozapine is licensed only for use in cases of schizophrenia which have failed to respond adequately to at least two different conventional neuroleptics. This restriction, together with the requirement for haematological monitoring and the relatively high prescription cost, has meant that its use is in general confined to a relatively severely affected subgroup of people with schizophrenia. In the USA, Meltzer *et al* (1993) have shown that the use of clozapine was associated with a mean reduction in annual cost of at least US$8000 per patient, due primarily to the reduction in frequency of hospitalisation of patients on clozapine. This study included those who were commenced on clozapine but dropped out of treatment, and accommodation costs and production losses incurred by family members. Three previous studies (Honigfeld & Patin, 1990; Revicki *et al*, 1990; Reid *et al*, 1994) in the USA reported larger cost reductions, of US$15 000–50 000; however, these did not include the indirect costs or those who had discontinued clozapine. There are substantial variations in the unit costs for health, social services, employment, and accommodation sectors between countries; caution must therefore be exercised in translating the significance of the above results to the UK.

Model-based evaluations (Davies & Drummond, 1994; Matheson *et al*, 1994) suggest that substantial savings could be accrued with the use of clozapine in the UK. We have performed a UK clinic-based study of the cost-effectiveness of clozapine, using clinical ratings and comprehensive costing methodology. In cost-effectiveness analysis, the costs of achieving outcomes using alternative treatment routes are estimated (Maynard, 1993): the outcome provided by treatment A per total cost under treatment A is compared with that provided by treatment B per total cost under treatment B. As it is necessary for the comparison to use the same outcome measure (e.g. quality of life) in the case of both treatments, this mode of economic evaluation is particularly applicable to studies relating to the use of two different treatment modalities for the same population.

METHOD

Data were collected covering the three years prior to commencing ('pre-') clozapine to the period following establishment of ('post-') clozapine therapy (minimum of one year,

†See editorial pp. 103–104, this issue.

https://doi.org/10.1192/bjp.171.2.125 Published online by Cambridge University Press

Table I Relevant characteristics of the cohort of patients on clozapine

Characteristic	Mean (s.d.)	Range
Age (years)	36.6 (9.59)	23–61
Age at onset of illness (years)	21.6 (5.23)	15–35
Duration of illness pre-clozapine (years)	10.7 (6.27)	1–25
Clozapine dose (mg)	522 (155)	300–800
Total number of hospitalisations pre-clozapine	6.5 (5.85)	2–33
Number of re-hospitalisations post-clozapine	0.4 (0.56)	0–2
Pre-clozapine informal carer time (hours/week)	6.9 (9.23)	0–25
Post-clozapine informal carer time (hours/week)	7.0 (9.07)	0–25
Pre-clozapine employment status[1]	0.4 (0.90)	0–3
Post-clozapine employment status[1]	1.3 (1.59)	0–5

1. Employment status coded as in Table 7.

mean 36.4 months) for 26 consecutive clozapine clinic registrants with DSM–III–R chronic schizophrenia (24) or schizoaffective disorder (2). Three also had a degree of learning disability (2 mild, 1 moderate). Most patients spent the greater part of their time in the community during the post-clozapine period. Two patients failed to continue on clozapine treatment (dropped out at 3 and 6 months due to noncompliance with monitoring, and problems related to moving out of the area), and were included in the cost analysis in order to avoid bias in favour of cost savings. The sample characteristics are shown in Table 1. There were 19 male and seven female subjects; 17 of Caucasian origin, eight of Afro-Caribbean origin, and one of mixed race. All had started clozapine because of inadequate therapeutic response to conventional neuroleptics; four cases were additionally intolerant to the neuroleptic medication.

Four clinical assessment scales were applied: the Global Assessment Scale (GAS; Endicott *et al*, 1976), the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962), the Quality of Life Scale (QLS; Heinrichs *et al*, 1984), and the Abnormal Involuntary Movements Scale (AIMS; Department of Health, Education and Welfare, 1974). The QLS is a 21-item scale based on a semi-structured interview designed to assess deficit symptoms in schizophrenia, in four categories (intrapsychic symptoms, interpersonal interactions, instrumental role functioning, and possession of common objects or involvement in common activities). Any adverse effects attributable to clozapine, periods of interruption of treatment, and the use of adjunctive medication were also documented. The clinical ratings were applied while the patients were on clozapine by interviewing patients and their principal carers (to determine the 'post-' values); the pre-clozapine values were determined retrospectively at the same interview with corroborative evidence from medical and nursing records.

Service and living costings

Periods of hospitalisation, out-patient service use, income and accommodation data were collected retrospectively using the Client Service Receipt Interview (Beecham, 1995) by interviewing either the principal carer (keyworker in the community or family member), or the client themselves, or both. Hospitalisations were costed for various types of psychiatric unit (forensic, adult general, etc.) per occupied bed day using figures estimated by the Maudsley and Bethlem Royal Accounts Department, or, for periods spent outside this NHS trust, the unit cost given in Netten (1994). Individual specialised community residences were approached in order to determine the cost per week of providing care, while the weekly costs attributable to the living costs of patients in private accommodation were calculated from estimates given by carers plus details of benefits received (direct costs incurred by carers therefore included). All costs were expressed at 1993–1994 price levels (£ sterling).

Details concerning usage of the following services were obtained: ward day patient service, community day centre, psychiatric out-patient service, and nurse-run depot clinic or clozapine clinic (including pharmacy, pathology, nursing, and medical staff time). The time spent by seven different types of health professional – psychologists, community psychiatric nurses, social workers, probation officers, occupational therapists, dietitians and general practitioners – was also documented. The unit cost estimates for these services (best estimates of long-term marginal opportunity costs; Beecham, 1995) were derived from information from the Maudsley and Royal Bethlem Hospitals NHS Trust Accounts Department, the individual hospital departments concerned, and from Netten (1994). For example, a unit cost for an attendance at a psychiatric out-patient service included the cost attributable to medical, nursing, and reception staff time, plus the overheads as calculated in a manner relevant to the cost of the addition of one client to an existing service; the unit cost of the clozapine clinic included the pharmacy, pathology, nursing, and medical costs calculated in a similar manner. Prescription costs were also calculated individually for each patient, including the costs of depot preparations, clozapine, and risperidone (with dosage and frequency of administration documented). The costs of other oral medications were not included, as this information was not readily available across the whole time period, and, owing to the much lower average cost of such drugs, was not estimated to be a significant contributor to the overall cost figures.

The time spent per week by informal carers and the employment status of the clients were noted across the time period. The employment status was assigned a grade on a five-point scale ranging from unemployment to full-time employment. Monetary figures were not assigned to these data due to the difficulty in assigning accurate values in these categories; it was felt to be more informative simply to give the raw data. Cost data were not available in sufficient detail to be included in the analysis for two subjects (both of whom showed a 20% improvement in their QLS scores). Cost-effectiveness (ratio of outcome achieved to cost) was calculated as QLS score divided by the total cost per year ($\times 10^{-4}$ for ease of calculation).

RESULTS

The clinical outcomes are shown in Table 2. Eighty-five per cent of the patients were at least 20% improved on BPRS and QLS ratings, with 69% showing a 20-point improvement in the GAS score. (A reduction in BPRS score reflects a reduction in symptomatology, while increase in the QLS and GAS scores reflect improvement in quality of life attained and global functioning, respectively.) The degree of improvement in all four of the clinical ratings reached statistical significance ($P<0.001$ on paired t-test,

https://doi.org/10.1192/bjp.171.2.125 Published online by Cambridge University Press

Table 2 Clinical ratings pre- and post-clozapine treatment (n=26)

Scale[1]	Pre-clozapine	Post-clozapine
	Mean (s.e.m.)	Mean (s.e.m.)
BPRS	67.5 (2.4)	43.6* (2.4)
QLS	24.0 (3.2)	54.2* (4.4)
GAS	28.7 (1.7)	48.7* (2.5)
AIMS	6.6 (1.1)	1.8* (0.8)

1. Details in text.
*P<0.001 on paired t-test.

results for all ratings satisfied tests for normality).

Table 3 shows the in-patient service usage prior to and after commencement of treatment with clozapine (mean date of commencement: February 1992). The most expensive type of in-patient service was intensive care psychiatry. The mean values for forensic psychiatry in-patient days per annum include two patients who were continuously hospitalised for the three years prior to clozapine commencement (i.e. mean of 365 days per year), but who, on clozapine, had spent 20 months out of hospital (living in specialised hostels) by the end of the study period.

In Table 4 the mean frequencies per annum of usage of other types of services are listed. The mean cost per annum of the depot clinic was £165.96, while that of the clozapine clinic was £348.13 (the unit cost of the clozapine clinic is approximately double that of the depot clinic). In addition, the total calculated prescription cost pre-clozapine was £5075 per annum (mean £211.46 per patient per annum) and after commencement of clozapine was £67 924 (mean £2830.17 per patient per annum). The mean total service costs pre- and post-clozapine were £4401 and £7738 per annum, respectively (Table 6). The percentage of the total service costs in the pre- and post-clozapine periods attributable to a specialised clinic service is therefore comparable in the two periods (depot clinic 3.8%, clozapine clinic 4.5%); however, the prescription costs during the period of treatment with clozapine account for a substantially higher proportion of the total service costs (36.6%, compared with 4.8% in the pre-clozapine period).

Table 3 In-patient service usage

Service	Mean number of days per annum	
	Pre-clozapine	Post-clozapine
General adult psychiatry (non-BMT)	9.4	0
General adult psychiatry (BMT)	48.9	38.5
Intensive care psychiatry	9.1	10.2
Forensic psychiatry	62.9	38.7

BMT, The Bethlem and Maudsley Hospitals NHS Trust.

Table 4 Service usage[1]

Service	Mean attendances per annum	
	Pre-clozapine	Post-clozapine
General adult psychiatry, day patient	39.8	6.5
General adult psychiatry, out-patient	6.8	7.6
Day care (including occupational therapy)	34.6	85.2
Community psychiatric nurse	6.3	12.0
Psychologist	0	0.5
Social worker (community psychiatry)	2.6	3.0
Probation officer	1.1	1.3
General practitioner (surgery)	1.9	4.0
Depot clinic	23.7	0
Clozapine clinic	0	21.9

1. Only services used by at least 5% of the sample in either time period are listed.

The accommodation costs are given in Table 5. Definitions of the accommodation categories 1–5 are as follows: category 1 corresponds to a specialised mental health hostel (e.g. a forensic psychiatry hostel) with a high staff to client ratio and awake staff at night; category 2 corresponds to a specialised mental health hostel with on-site staff at night who are available on-call but not necessarily awake; category 3 corresponds to a sheltered housing complex with an on-site warden; category 4 to a group home with no on-site staff but staff available on-call; and category 5 includes various types of private or individual accommodation (family home, council flat, etc.). The ranges of costs given are the actual costs given by the residences in those categories; clearly there is overlap in weekly costs between the categories. Calculation of the total annual accommodation costs per patient across the time period was made from the actual figures supplied by the residences where possible; if these were not available, then the mean weekly cost for the appropriate category was used (based on data given by other hostels in the same category). The mean annual accommodation cost was £3131 pre-clozapine and £5358 post-clozapine (Table 6), owing to the greater proportion of time spent in the community (i.e. not as in-patients) by the subjects in the post-clozapine period, with an increase in the proportion of subjects living in relatively high-dependency units.

The total mean annual direct cost to the health, social, and private sectors for this sample of patients suffering from schizophrenia prior to their treatment with clozapine was £36 604; £3768 more than the corresponding total mean annual direct cost during their treatment with clozapine (£32 836) (Table 6). The relative proportion of the total cost attributable to service and accommodation cost increases in the post-clozapine period. Despite a near doubling in the total service cost (attributable mainly to the increase in prescription costs post-clozapine, as detailed above), and an increase in the accommodation cost to a lesser degree, the total cost falls owing to the reduction in hospitalisation cost of a mean of approximately £10 000 per annum. However, the difference between the pre- and post-clozapine total costs did not reach significance, and, indeed, it may be observed that with the exception of the accommodation costs, the 95% confidence limits of the mean pre- and post-clozapine values overlap. This may reflect the small sample size (n=24 for the cost data). None the less, if quality of life is considered, a highly significant improvement in cost-effectiveness of the comprehensive

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Table 5 Accommodation costs

Category[1]	Cost[2] (range)	Pre-clozapine[3]	Post-clozapine[3]
1	£289.63 (£270–300)	9	48
2	£199.33 (£144–300)	13	48
3	£112.00 (£104–120)	14	15
4	£125.00 (£81–169)	0	19
5	£73.22 (£50–140)	191	148

1. Categories detailed in text.
2. Cost given as mean weekly cost within each category, plus the range of costs for this sample in these categories of accommodation.
3. Pre- and post-clozapine data given as mean number of days per annum spent in each category of accommodation.

Table 6 Costs (£ sterling) pre- and post-clozapine and cost-effectiveness calculated as per text

	Pre-clozapine		Post-clozapine	
	Mean (95% CI)	% of total mean	(95% CI)	% of total mean
Hospitalisation	29 072 (15 138–43 006)	79.4	19 740 (9767–29 712)	60.1
Accommodation	3131 (2220–4042)	8.6	5358 (4212–6504)	16.3
Service use[1]	4401 (2389–6412)	12.0	7738 (6083–9392)	23.6
Total cost	36 604 (23 858–49 350)	100	32 836 (22 769–42 902)	100
Cost-effectiveness	15.2* (8.14–22.3)		33.0* (20.3–45.7)	

1. Includes in the pre-clozapine calculation depot medications (0.6%) and depot clinic (0.5%); includes in the post-clozapine calculation antipsychotics (8.6%) and clozapine clinic (1.1%).
*$P<0.005$ on paired t-test.

Table 7 Employment status before and after introduction of clozapine

Employment	Code	Number of subjects	
		Pre-clozapine	Post-clozapine
Unemployed/in-patient	0	21	12
Sheltered work	1	2	5
Voluntary work	2	1	4
Student	3	2	2
Part-time work	4	0	1
Full-time work	5	0	2

services offered is demonstrated; the cost-effectiveness during the post-clozapine period (33.0) is more than double that in the pre-clozapine phase (15.2).

Table 7 illustrates the improvement in employment status of the subjects during clozapine treatment. Two subjects attained full-time employment during the study period. One of these had previously managed only voluntary work, the other had made several unsuccessful attempts to start courses as a student. There is a significant increase in the mean employment status of the subjects while on clozapine (Table 1, $P<0.001$, paired t-test), with a non-significant increase in the hours per week provided by informal carers such as family members. Therefore, although monetary values were not assigned to these data, it would be expected that there would be a net gain in the indirect (productivity) costs during the post-clozapine period.

Clozapine treatment was associated with a significant reduction in involuntary movements as documented by the AIMS score. The seven most common side-effects experienced by the patients while on clozapine were as follows (percentage of patients affected in brackets): weight gain (77%), drowsiness (65%), sialorrhoea (62%), constipation (54%), orthostatic symptoms (31%), akathisia (31%), and tachycardia (23%). After the initial one to two months during which side-effects were particularly troublesome, many of our patients seemed able to tolerate the adverse effects, and recognised their improved quality of life – there were no cases of non-compliance due to adverse effects during the period of treatment with clozapine, and no cases of agranulocytosis. There were three interruptions of clozapine treatment for the following reasons: transient neutropenia to 1.43×10^{-9}/l, which resolved spontaneously; a six-month interruption due to delta waves over the left temporal lobe on EEG accompanied by highly disturbed behaviour; and a tachycardia with hypertension to 150/100 mmHg which did not recur when clozapine was restarted more gradually. Only two discontinuations occurred, due to noncompliance with haematological monitoring, and funding difficulties after moving out of our area. The latter recommenced clozapine subsequent to the termination of the study period.

The following medications were used in combination with clozapine in a total of 12 clients (46%): oral antipsychotics (haloperidol, chlorpromazine or risperidone, $n=5$), sodium valproate (one with epilepsy diagnosed prior to commencing clozapine, one when clozapine was restarted after the EEG abnormality detailed above), lithium carbonate (the subject with schizoaffective disorder), amitriptyline (for sialorrhoea, $n=4$), and propranolol (as an anxiolytic, $n=1$). Of note less than 20% of our clients received adjunctive antipsychotic medication, while the overall response rate to clozapine as defined by the BPRS and QLS scores was 85%.

DISCUSSION

This study included retrospective collection of data, and was not conducted in the manner of a formal, cost-effectiveness clinical trial: it was a naturalistic study of a cohort of patients on clozapine in a routine clinical setting with a mirror-image design. It may be argued that a naturalistic study is able to give information that is more clinically applicable than similar research conducted in the setting of a clinical trial. As a clinic-based study, it could be suggested that a selection bias in favour of responders was operating, but of note both attenders and non-attenders of the clinic were included (subjects were consecutive clinic registrants).

The small sample size is an obvious limitation. We decided that a detailed clinical and economic analysis on a small sample might give more informative results than a less detailed study on a larger sample.

https://doi.org/10.1192/bjp.171.2.125 Published online by Cambridge University Press

Table 8 Sample characteristics compared with those of Meltzer *et al* (1993) and Kane *et al* (1988)

Characteristic	Kane *et al* (*n*=319) Mean (s.d.)	Meltzer *et al* (*n*=37) Mean (s.d.)	Present study (*n*=26) Mean (s.d.)
Age (years)	35.7 (8.87)	31.5 (6.9)	36.6 (9.59)
Age at onset (years)	20.4 (4.61)	20.7 (7.9)	21.6 (5.23)
Number of hospitalisations pre-clozapine	9.2 (7.26)	8.1 (7.3)	6.54 (5.85)
Baseline BPRS	61.0 (12.0)	51.1 (12.3)	67.5 (12.1)
Baseline QLS	Not available	29.7 (20.0)	24.0 (16.3)

As can be seen from Table 8, the mean values and standard deviation for the age when studied, age at onset, and number of hospitalisations pre-clozapine were very similar for our sample to the values for the 37 patients in the study by Meltzer *et al* (1993) for whom cost data were available and the 319 patients in the seminal multi-centre trial by Kane *et al* (1988). It would, therefore, appear that in these respects our small sample is representative of the total population of patients treated with clozapine.

The greatest proportion of the total costs during the period subsequent to commencement of clozapine was incurred in our study during the first year of clozapine treatment (data not shown); if the study had been continued for longer, the mean post-clozapine cost values would therefore be predicted to be substantially less. An alternative design, comparing costs associated with the treatment of patients with conventional neuroleptics at least one year after commencement of treatment, with costs associated with clozapine again at least one year after commencement of treatment, would have yielded apparently greater cost savings. Indeed, in the study by Meltzer *et al* (1993), the costs associated with the index hospitalisation (admission during which clozapine was commenced) were excluded.

We appear to have a particularly high response rate (85% showing an improvement of at least 20% on BPRS and QLS ratings, with 69% showing a 20-point improvement in GAS ratings). As the post-clozapine scores for the BPRS, GAS and QLS differed equally significantly from their pre-clozapine counterparts ($P<0.001$), it was not considered necessary to incorporate the BPRS and GAS ratings in the outcome component. Other more stringent criteria may be employed for response, e.g. an improvement of at least 20% on the BPRS plus a post-treatment BPRS total score of 35 or lower (the criteria employed by Kane *et al*, 1988); using these criteria our response rate was only 31%. This may reflect the relatively high pre-treatment BPRS values in our sample (Table 8), so that although a significant reduction is attained by the majority of the sample, only 31% had a BPRS falling to 35 or lower. Other studies show a response rate of between 30 and 76% by these criteria (Kane, 1992; Lieberman *et al*, 1994).

It could be argued that the improved outcome and cost reduction in the post-clozapine period should be more correctly attributable to factors other than the change in medication (i.e. that the apparent improvement on clozapine was merely a 'halo effect'). For example, the reduction in hospitalisation periods might be attributable to changes in the hospital admission policies during the study period or to an enhancement in the provision of community services. However, excluding the index admission, our mean length of stay prior to clozapine treatment was 96.5 days (*n*=44 admissions), with the mean length of stay on clozapine being 132.8 days (*n*=four admissions, cases with no re-admissions excluded). The very low re-admission rate is shown in Table 1; the clinical ratings and other data such as the employment status during the period of treatment with clozapine indicate that the majority of this sample would not warrant admission even if relatively loose admission criteria were employed, and most were not receiving intensive community service input.

The effect of the clozapine clinic must also, however, be considered; in our clinic, adverse effects are monitored, and dose adjustments or the addition of appropriate adjuvants made, together with psychoeducation to enhance understanding of the role of clozapine and hence compliance. Since the completion of the study, the frequency of haematological monitoring required has decreased to once monthly for patients prescribed clozapine for at least a year who have had no prior abnormal haematological results. Further, it is now possible for general practitioners to prescribe clozapine, with patients collecting clozapine from the local pharmacy. If a similar study to ours were conducted either in a hospital setting with patients who had been registered for clozapine for at least a year, or in a general practice setting on a similar population of patients, information regarding the relative magnitude of the contribution of a clozapine clinic service to the outcome might be gained.

We calculated our cost data using actual 1993–1994 costs and actual attendance figures. Unlike the early studies conducted in the USA, data on the clozapine discontinuers (or 'drop-outs') was included. The data also include the social services and private sector direct costs as well as those incurred by all relevant sections of the health service, with detailed documentation of the components of the cost calculation, including the categories of accommodation (not given in Meltzer *et al*, 1993). Details relevant to the indirect costs attributable to changes in productivity have been presented in a manner that allows readers to draw their own conclusions. We suggest that our study provides valuable data on the cost-effectiveness of clozapine in the UK, and may warrant replication using similar methodology in a larger sample.

Similar methodology might also be applied to the investigation of the cost-effectiveness of another atypical antipsychotic. A study applying UK costs (1993–1994) to 31 patients treated with risperidone in Sweden in the early 1990s found that in those for whom cost data were available for two years, there was a reduction in mean direct cost of £7426 per patient (Guest *et al*, 1996). This study was similar to ours in that it was a mirror-image design; however, the figures for the discontinuers were not included in the overall costs, and the full range of services costed in our study were not included, neither are any data provided regarding contributors to indirect costs. Moreover, as the pattern of resource distribution and allocation may differ significantly between different countries, it may be difficult to draw conclusions from a report in which UK costs were applied to Swedish data. We suggest that the application of our methodology to a UK study involving risperidone could yield useful results.

Of note, in our study, the local costs attributable to haematological monitoring required for the administration of clozapine

https://doi.org/10.1192/bjp.171.2.125 Published online by Cambridge University Press

(i.e. the clozapine clinic service) accounted for a near comparable percentage of the total service costs as those attributable to the depot clinic, with the bulk of the increased service cost in the post-clozapine period comprising the increased prescription cost of clozapine. Hence, if the prescription cost of a given atypical is comparable to that of clozapine, it would be expected to be similar in cost-effectiveness if demonstrated to be associated with a change in quality of life of equal magnitude in a similar patient group. This prediction ignores the possible confounding variables such as the positive therapeutic effect of regular attendance at a clozapine clinic.

Olanzapine (at doses of 5–20 mg per day) has been claimed to have a superior effect on quality of life over haloperidol (also at 5–20 mg per day) over a 52-week treatment period (Martin, 1996). The prescription costs for olanzapine are, however, significantly higher than for haloperidol; in order to attain superior cost-effectiveness over haloperidol, olanzapine would have to be associated with a substantially superior improvement in quality of life. There are as yet no data comparing the efficacy of olanzapine and clozapine on quality of life. A naturalistic study comparing the cost-effectiveness of clozapine administered in the community by general practitioners with that of olanzapine after at least a year of treatment could yield informative results.

With schizophrenia representing a major disease burden in terms of NHS expenditure (Department of Health, 1996), there is a need to determine whether or not certain treatments are more cost-effective than others, especially when applied to the more severely affected patients.

CLINICAL IMPLICATIONS

- Despite high prescription and monitoring costs, clozapine may be more cost-effective than typical antipsychotics in treatment-resistant schizophrenia.
- Clozapine was clinically effective in a group of people severely affected with schizophrenia, causing significant improvement in quality of life, paralleled by significant improvement in employment status.
- Further community-based studies comparing the cost-effectiveness of clozapine with that of other atypical antipsychotics are warranted.

LIMITATIONS

- The sample size was small (n=26).
- This was an open study.
- Pre-clozapine data were collected retrospectively.

ACKNOWLEDGEMENTS

This study was unsponsored. However, we thank the patients and staff of the Maudsley and Bethlem Royal Hospitals NHS Trust, Professor M. R. J. Knapp and Dr P. Sham for methodological and statistical advice, Dr L. Pilowsky for assistance in data analysis, and Mr D. Taylor for helpful comments on the manuscript.

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(Received 8 November 1996, accepted 7 February 1997)

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https://doi.org/10.1192/bjp.171.2.125 Published online by Cambridge University Press