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The cost of relapse in patients with schizophrenia in the European SOHO (Schizophrenia Outpatient Health Outcomes) study

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ABSTRACT

Background: Relapse in schizophrenia is one of the greatest burdens of the illness.
Aims: To estimate the costs associated with relapse in a pan-European naturalistic setting.
Method: The SOHO study is a 3-year, prospective, observational study of 10,972 outpatients with schizophrenia across 10 European countries. The cost of resource use (inpatient stay, day care, psychiatrist visits and medication) for those who ever relapsed in three years was compared to those who never relapsed. One-year costs for both groups were also compared for a more stringent comparison. The analyses were adjusted for patient characteristics and took account of non-normality of the cost data by using a log-link function. UK unit costs were applied to resource use. The analysis was repeated after multiple imputation for missing data.
Results: Costs incurred by patients who ever relapsed (£14,055) during three years were almost double to those incurred by patients who never relapsed (£7417). 61% of the cost difference was accounted for by hospital stay. The impact of relapse was even greater in the 1-year cost comparison. Results from the additional analysis with imputed missing data remained largely consistent.
Conclusions: Our findings confirm the significant economic burden of relapse, and show such costs were mainly due to hospital stay. Nevertheless, the use of UK unit costs requires caution when interpreting this costing in the context of a specific country, as resource use and their associated costs will differ by country.

1. Introduction

Schizophrenia is a chronic mental illness with serious physical, social and economic consequences (Buckley, 1998; de Sena et al., 2003). The annual economic burden of schizophrenia was estimated to be £6.7 billion in 2004/05 in England, of which the direct cost of treatment and care accounted for about 30% (£2 billion) (Mangalore and Knapp, 2007). The burden of indirect costs — mainly because of lost productivity due to unemployment, absence from work and premature mortality of patients — was shown to be even greater, amounting to nearly £4.7 billion. A review of the international cost-of-illness studies also revealed (Knapp et al., 2004) an equally sizable economic burden of the illness.

Much of this cost burden can be attributed to the consequences of relapse (Weiden and Olfson, 1995). The majority of patients with schizophrenia typically experience acute symptomatic relapses alternated with durations of full or partial remission over a period of many years (de Sena et al., 2003). Specialist psychiatric hospital admission and targeted treatments are often required during periods of acute relapse, which leads to significant resource demands on health care and social care systems (Beard et al., 2006). In addition, frequent relapses can cause progressive functional deterioration, worsening treatment response and clinical prognosis (Csernansky et al., 2002; Pompili et al., 2007), which would in turn increase both direct and indirect costs of the illness. Just a decade ago in the United States, Weiden and Olfson (1995) estimated the cost of relapse to be about $2 billion (at 1993 price) just for hospital readmission. Rather surprisingly however, there is only limited information on the actual costs of relapse in Europe. Many of cost estimates related to relapse have been drawn from economic evaluations of antipsychotics based on various assumptions.

The large prospective pan-European Schizophrenia Outpatient Health Outcomes (SOHO) study provides a unique opportunity to estimate the direct costs associated with relapse over a 3-year follow-up in routine clinical practice in Europe.

Abbreviations: CGI, Clinical Global Impression; CGI-SCH, Clinical Global Impression-Schizophrenia; HCHS, Hospital and Community Health Services; NHS, National Health System; PSSRU, Personal Social Services Research Unit; SOHO, Schizophrenia Outpatient Health Outcome; TFR, Trust Financial Returns.

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2. Methods

2.1. Patient recruitment

The SOHO study was an international prospective observational study that was conducted in 10 European countries. One thousand and ninety-six investigators participated, who were psychiatrists working mostly in public (46.9%) or combined public and private (37.2%) practices. A total of 10,972 patients were enrolled. Recruitment by country was highest in Germany ($n=3449$ patients), Italy ($n=3016$ patients), Spain ($n=2053$ patients) and France ($n=964$ patients). The remaining 1490 patients were enrolled in Denmark ($n=38$ patients), Greece ($n=766$ patients), Ireland/the UK ($n=344$ patients), the Netherlands ($n=177$ patients), and Portugal ($n=175$ patients). The study was approved in all countries either at the site, regional, or national level, depending on the country and local regulations. Patient consent followed country regulations. All patients gave at least oral informed consent and written informed consent was obtained in Denmark, Italy, Portugal, Spain, Ireland and the UK. Participating psychiatrists offered enrolment to patients who met the following entry criteria: initiating or changing antipsychotic medication for the treatment of schizophrenia (according to DSM-IV or ICD-10 diagnostic criteria and/or clinical judgement); presenting within the normal course of care in the outpatient setting or in the hospital when admission was planned for the initiation of antipsychotic medication and discharge planned within 2 weeks; at least 18 years of age; and not participating in an interventional study. Patients were included regardless of the reason for treatment change and regardless of whether an antipsychotic drug was being initiated as a replacement for a previous medication, was an addition to existing treatment, or was being initiated for the first time or after a period of no treatment.

As the original design of the study was to focus on the outcomes of patients treated with olanzapine compared with other antipsychotic treatments, the study was designed to provide two cohorts of patients of approximately equal size by oversampling patients starting olanzapine: (1) patients who initiated therapy with or changed to olanzapine; and (2) patients who initiated therapy with or changed to non-olanzapine antipsychotic. Enrolment was thus conducted in a systematic alternating order in most countries; the first patient was recruited into the olanzapine cohort, the next patient was recruited into the non-olanzapine cohort, etc. All patient care during the study period was at the discretion of the participating psychiatrist. In order not to alter prescription practices, no minimum number of patients was required to be enrolled by each participating investigator and the enrolment period was purposely long. There were no instructions regarding medication treatment in the study description. The participating psychiatrists could prescribe medication and change it at any time following their usual practice. Patients remained in the study regardless of any medication change after baseline.

Data collection for the study occurred during visits within the normal course of health care. The routine outpatient visit at which patients were enrolled served as the time for baseline data collection. Subsequent data collection was targeted for 3, 6, 12, 18, 24, 30 and 36 months. For each data collection target, investigators were allowed to collect data up to one month before or after the target month. Patients who were not seen during the normal course of care within one assessment interval were not excluded from subsequent data collection.

Clinical severity was assessed using a scale based on the Clinical Global Impression (CGI) (Guy, 1976), which evaluated positive, negative, cognitive, depressive and overall symptoms on the day of assessment (CGI-SCH) (Haro et al., 2003a,b). The CGI and CGI-SCH are physician-rated scales with values ranging from 1 (not ill) to 7 (among the most severely ill patients). Compliance was also assessed by the participating investigators using a single-item question rating scheme: (1) patient has not been prescribed antipsychotic medication during the prior 4 weeks; (2) patient almost always complies/adhere to antipsychotic medication treatment; (3) patient complies/adheres to antipsychotic medication treatment about half of the time; and (4) or patient almost never complies/adheres to antipsychotic medication treatment.

Further details about the design of the SOHO study have been provided elsewhere (Haro et al., 2003a,b, 2005).

2.2. Definition of relapse

Relapse is usually defined as a significant increase in symptom severity, decrease in social functioning or change in the pattern of care such as hospitalisation (Lader, 1995; Robinson et al., 1999). In the present study, relapse was defined as an increase in the CGI-overall severity score; or having had a hospitalisation. To qualify for relapse, the increase in the CGI-overall severity score has to be at least 3 points when the minimum score for that patient during follow-up was 1 (not ill), at least 2 points when the minimum score was 2 (borderline ill) or 3 (mildly ill); or at least 1 point when the minimum score was 4 (moderately ill), 5 (markedly ill) or 6 (severely ill). By including hospital admission in the definition of relapse, the cost of relapse was going to be higher due to admission costs. Thus, a sensitivity analysis was conducted defining relapse only in terms of the increase in the CGI-overall severity score (i.e. no requirement for hospitalisation).

2.3. Resource use and associated costs

The following resource uses were recorded at every visit: the number of schizophrenia-related admissions and inpatient days; the number of schizophrenia-related day hospital or day care centre days; and the number of schizophrenia-related outpatient consultations with a psychiatrist. In addition, the type and dose of antipsychotic drugs prescribed and the type of concomitant medications taken (anticholinergics, antidepressants, anxiolytics/hypnotics or mood stabilisers) were also obtained.

UK unit costs were applied to the pan European resource use data. UK unit costs were used because of their quality and availability. Unit costs for an inpatient day, day hospital/day care visits and outpatient psychiatric consultation were taken from the Personal Social Services Research Unit (PSSRU) unit cost volumes (Netten and Curtis, 2002, 2003), which in turn were based on the Trust Financial Returns (TFR2) specialty and programme cost returns to the UK Department of Health by NHS Trusts. The costs referring to the mental health specialty were inflated to include an element of capital costs based on the schemata published by Netten and Curtis (2002) and inflated to 2005 price levels using the Hospital and Community Health Services (HCHS) Pay and Prices Index (Netten and Curtis, 2005).

The cost per mg of each antipsychotic drug was estimated from the Monthly Index of Medical Specialties (MIMS, 2005) and the Chemist and Druggist Supplement (CMP Medica Ltd, 2005). Where an antipsychotic had more than one form of packaging, the relative retail market shares for the UK were used to weigh the average price per mg using the IMS Health MIDAS® database (IMS Health Inc., Q2/2005).

Where patients received concomitant medications, the average daily cost of anticholinergics, antidepressants, anxiolytics/hypnotics, or mood stabilisers was taken from the IMS Health MIDAS® database and weighted by the retail market share in the UK also provided by the IMS Health MIDAS® database (IMS Health Inc., Q2/2005).

We assumed that patients receiving clozapine underwent haematological monitoring (differential and white blood cell count) prior to treatment initiation, weekly for the first 18 weeks of treatment and fortnightly thereafter. Patients co-treated with the mood stabilisers lithium, valproate or carbamazepine were assumed to have their drug plasma levels monitored as well as a complete blood cell count taken 2.5 times per annum. The costs of the tests were taken from the Pharmaceutical Industry Costing Analysis System (PICAS®) database.