Cost of Treatment of Schizophrenia in Six European Countries

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Abstract

Background and aims:
As part of a RCT in six European sites, the direct mental health care cost for 422 patients with schizophrenia was analysed according to how total, and medication costs differed across sites and which variables were likely to predict total or service-specific costs.

Method: Service use was recorded continuously during a 12-month follow-up. Prescribed psychotropic medication was recorded at baseline and 12 months later. Service use data were transformed into EURO, log-transformed and analysed using linear regression models.

Results:
Although samples were homogeneous, large inter-site cost differences were found (annual means ranging from 2,958 € in Spain up to 36,978 € in Switzerland). Psychopharmacologic costs were much more constant across sites than costs for other services. Total costs were associated more with region or socio-demographic characteristics than with disorder related parameters.

Conclusions:
The findings confirm remarkable differences in direct costs of patients wit schizophrenia across Europe. However, the relative stability of medication costs suggests a need to analyse mechanisms that influence service specific costs for schizophrenia.

Keywords
schizophrenia, community care, service utilization, cost of care, psychopharmacologic costs

1. Introduction

Research on the costs of care for patients suffering from schizophrenia has increased during recent years. However, evidence is still scarce, as most studies target only selected aspects of the wide range of treatments or services provided for patients with schizophrenia. A considerable proportion of research focuses on psychopharmacological treatment regimes and their economic consequences. This was stimulated by the need to evaluate whether or not the prescription of costly second-generation neuroleptic drugs, which were increasingly launched throughout the 1990s, is cost-effective in routine care. However, many of these cost-effectiveness studies preferred a decision model approach, feeding selected administrative, epidemiological, or clinical data into decision trees. The appropriateness of this approach is an issue of recent controversial debate (Hansen et al., 2006; Beard et al., 2006; Barbui & Lintas; 2006). Follow-up studies assessing and analysing psychopharmacologic drug consumption and the associated costs from a naturalistic perspective on a patient level are still scarce. Rarer still are cross-country comparisons that address total cost of care for patients suffering from schizophrenia with a particular focus on medication costs, as in this case, the diversity of international community mental health care models has to be controlled for. Such an approach multiplies the methodological problems. Among the factors to be considered are varying price levels and funding mechanisms for mental health care, which are even more complex than the various community care concepts (Knapp et al., 2003; Windmeijer et al., 2006).

Thus, very few macro-level comparisons of the cost of care for patients with schizophrenia across European countries are available to date, e.g., the EPSILON study (Knapp et al., 2002), that compared service utilization and cost profiles of people with schizophrenia living in five European locations. The study found higher needs, greater symptom severity and longer psychiatric history being associated with higher costs. However, most of cost studies in this field often fail to link costs to outcomes of care, and they do not necessarily specify the cost of psychopharmacological drug use. In the face of recent doubts about the cost-effectiveness of second-generation antipsychotics informed by controversial findings from various trials and meta-analyses (Rosenheck, 2006; Rosenheck et al., 2006; Jones et al. 2006; Davies et a.l. 2008; Zhu et al. 2008; Carpenter & Buchanan 2008), quantitative data in this field are fundamental to the ongoing transformation of community care systems. To bridge this gap, we analysed the total cost of care for patients with a diagnosis of schizophrenia in six countries as a part of a randomised controlled European trial, in which particular emphasis was put on the prospective recording of the cost of psy-

chopharmacologic drug use on the patient level. The following research questions were addressed:

- What are the overall costs and service-specific costs of care for patients with schizophrenia in the six sites and how do these differ across sites?
- What variables predict total and service-specific costs of care across the sites?

2. Material and Methods

2.1 Study

This randomised controlled trial was conducted in community psychiatric services in Granada (Spain), Groningen (the Netherlands) London (UK), Lund (Sweden), Mannheim (Germany) and Zurich (Switzerland), covering urban and mixed urban-rural areas.

The original trial hypothesised that regular use of a novel computer-mediated procedure (called DIALOG) in routine meetings between clinicians and community patients with schizophrenia would be associated with a more favourable quality of life, fewer unmet needs for care, and higher treatment satisfaction after a one-year period as opposed to treatment as usual. By applying DIALOG, clinicians discussed regularly eleven life and treatment domains with the patients in the experimental group and asked them to rate their satisfaction with each domain. The rating was followed by a question as to whether the patients wanted any additional or different help in the given domain. The control group patients continued with standard treatment. The study design, study sample, settings, aims, and primary outcomes are described in detail elsewhere (Priebe et al., 2002; Priebe et al., 2007).

In order to analyse the costs of mental health care for participating patients, the assessments included a detailed prospective recording of mental health service use covering a 12-month follow-up period. Additionally, for each patient the prescription of psychotropic medication (including type of drug, brand name, daily dosage and dosage form) was recorded at baseline and again 12 months later.

The prime objective of the cost analyses (based on the service use and medication data) was to determine and analyse the total mental health care costs and service-specific costs, including psychopharmacologic drug cost for patients across all sites. In a second step, predictors of the cost of care were analyzed.

2.2 Inclusion criteria

Clients who met the following inclusion criteria were identified: living in the community (not 24-hour assisted accommodation) and treated as outpatients by community mental health teams; at least 3 months of continuous care in the current service; capable of giving informed consent; sufficient knowledge of the language of the host country; a primary diagnosis of schizophrenia or related psychotic disorder (ICD-10 = F20-F29); aged between 18 and 65 years of age (to constrain the sample to the core group of community psychiatry and exclude patients suffering from co-morbidity such as somatic diseases or dementia); meeting with their key worker at least once every two months, with the expectation that they would continue with the service for the next 12 months; and absence of severe organic psychiatric illness or primary substance abuse. Written informed consent was obtained from all patients participating in the study.

Pre-intervention data collection was from December 2002 to September 2004, and post-intervention data was collected from December 2003 to May 2005. Patients were interviewed at both time points by trained researchers (psychologists who did not belong to the clinical teams that were responsible for the treatment of patients), either at the relevant community mental health service or at home. The interviews included the whole set of scales and instruments as described below (see assessments). The psychologists were not blinded whether patients were in the experimental or control group.

Organisational Characteristics of Services involved

The population size of the involved catchment areas varied (Granada: 188,000 inhabitants; Groningen: 400,000; London: 710,000; Lund: 100,000; Mannheim: 320,000; Zurich: 382,000). Although all included countries adopted community mental health care as a basic concept for treating patients with schizophrenia, the actual provision of inpatient, outpatient or rehabilitative services differed considerably from region to region, according to national characteristics of mental health care delivery or other factors.

Granada, where 3 community mental health teams (CMHT) with a total of 19 staff members were provided to serve the patients with schizophrenia of the catchment area, was the least well equipped region in terms of CMHTs, psychiatric hospital beds (0.10-0.11 per 1,000 population) or places in sheltered accommodation (0.08 per 1,000 population). *Groningen* had 4 CMHTs with 55 staff members, a psychiatric bed rate of ca. 0.4 per 1,000 population and ca. 0.10 sheltered accommodation places per 1,000 population. The East London site, which collaborated in the stud offered 267 psychiatric hospital beds (0.37 per 1.000 population). Outpatient care in London was provided by 10 CMHTs with a

total of 400 staff members. In *Lund*, there were 4 CMHTs with 15-18 staff members each. The psychiatric bed rate of the Lund catchment area was 0.85 per 1,000 population and places in sheltered accommodation were 0.53 per 1,000 population. Outpatient mental health care in *Mannheim* and *Zurich* differed from the other centres, as in Germany and Switzerland, numerous private psychiatrists in office practice (whose treatments are covered by the Swiss or German health insurance schemes and were not disproportionally more expensive against those provided by outpatient departments) are strongly involved in outpatient mental health care. In the Zurich region alone, approx. 200 psychiatrists are based in office practice (ca. 0.5 per 1,000 population). Compared to other countries, this dense network of outpatient psychiatrists diminishes the role of German or Swiss CMHTs to a certain degree. On the other hand, rehabilitative and residential care is a major sector of mental health care both in Switzerland and Germany, where places in sheltered accommodation mounted to 0.52 (Mannheim) and 1.05 (Zurich) per 1,000 population. Mannheim had 0.52 psychiatric hospital beds per 1,000 population, whereas the rate in Zurich was 0.78.

The average case-load of a CMHT-keyworker varied also. It ranged from 8 (Zurich) 10-12 (Mannheim, London), to 18.5 (Groningen) and 25 (Lund). Case-loads in Granada were probably much higher, but unfortunately case-load figures from Granada were not available. Usually, CMHTs include part- or full time psychiatric nurses or social workers. Psychiatrists or psychologists are part of the teams in most, but not in all countries (e.g. for reasons mentioned above, not in Switzerland or Germany). Some teams add additional professions e.g. occupational or other therapists, while others do not provide such services. CMHTs usually are responsible for health care planning and coordination, case management, supportive counselling, the prescription or application of psychotropic medication, psychotherapy, home visits or other services. Again, this differs with the national mental health care principles or concepts and and the capacities of regional services.

These capacities and rates must be seen as rough estimates, as inpatient or outpatient capacities of catchment areas are rarely selective and tend to overlap with neighbouring regions. Additionally a variety of additional rehabilitative services not mentioned here may contribute to the various community care systems, so that the effectiveness of such core services as CMHTs is hard to assess from the size, composition or case-loads of the teams alone. Nevertheless, these figures suggest that community mental health care in the 6 countries provide somewhat different care on the ground.

This cost study recorded all contacts of patients with mental health care services in the respective region, not only those to services described above to characterize the different community care concepts.

2.3 Study sample

The original RCT included a total of 507 patients. Their key workers were randomly assigned to either the intervention or control condition in order to avoid potential contamination between intervention groups. Key workers were randomized with the use of a computer generated random block number allocation sequence (to ensure an equal balance across sites). The randomization procedure was completed separately by each country, per CMHT and was stratified by professional background (Community psychiatric nurse, social worker, support worker etc.) and by the number of patients within each key worker's caseload that consented to participate.

Overall, the intervention group included 271, the control group 236 patients. Of these patients, 451 completed the follow-up. Detailed socio-demographic and morbidity data are reported elsewhere (Priebe et al., 2007). Due to the randomised controlled trial design, there were no significant differences in the characteristics of participants in the control and intervention groups across all sites at baseline. Only patients with full 12-month coverage of utilisation data were included into the cost-analyses. Additionally to 57 drop-outs during the follow-up, another 29 patients had to be dropped from the final data set due to incomplete service use information (Granada 11, Groningen 0, London 7, Lund 3, Mannheim 6, Zurich 1). The final sample for cost analyses encompassed 422 patients.

2.4 Assessments

Clinical assessments as used in the original RCT to compare clinical outcomes in the control and intervention groups (Priebe et al., 2007) were seen as potential cost predictors and included into the cost analyses. These scales were used:

- the Manchester Short Assessment of Quality of Life (MANSA) (Priebe et al., 1999), on which patients rate their satisfaction with 12 life domains on a 7-point scale from 1 ('couldn't be worse') to 7 ('couldn't be better'). The mean score of all 12-satisfaction questions was used as a cost predictor.
- the 8-item Client Satisfaction Questionnaire (CSQ-8) (Nguyen et al., 1983) assessing clients' general satisfaction with services.
- the Camberwell Assessment of Need Short Appraisal Schedule, patient-rated version (CANSAS) (Slade et al.,1996) which assesses health and social needs across 22 domains, the CANSAS produces two subtotal scores: 'total unmet needs' and 'total met needs'.

- the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), a 30-item, 7- point scale from 1 ('absent') to 7 ('extreme'). The PANSS comprises a global score, and three subscales (positive, negative, and general psychopathology).

- Socio-demographic information and data on mastery, empowerment, self esteem, drug compliance, and other domains were also collected at baseline or during follow-up and used as potential cost predictors.

- Study clients' use of mental health care services was recorded continuously for twelve months with the Service Utilization Sheet (SUS), which adapted the service items and definitions of the Client Socio-demographic and Service Receipt Inventory (CSSRI) (Chisholm et al. 2000) and of the European Service Mapping Schedule (ESMS) (Johnson et al., 2000).

- Intake of psychotropic medication was assessed cross-sectionally at baseline and follow-up by recording the brand name and dosage of each psychotropic drug prescribed for each patient.

The 12-month psychotropic drug cost was estimated on the basis of the medication intake at baseline, assuming that possible changes in psychotropic drug prescription were levelled out across the sample and intake patterns at the group level remained more or less stable over time. Prior to assigning cost estimates, depot medication was converted into average doses of mg per day. To avoid double costing, intake and costs of psychotropic drugs were adjusted for inpatient stays, during which medication is covered by hospital fees or rates.

Patient-level cost profiles were calculated by weighting all service contacts during the follow-up with country- or centre-specific unit-cost estimates, which were derived from national data sources. To assign cost estimates for psychotropic drugs, the lowest national market price for the respective drug was used. All cost data was transformed into € as a single currency using conversion rates from January 1, 2004. To eliminate price-level differences between countries, PPP-conversion rates (power purchase parities) were used, the S]TJ0.00079 Tc 0.03011 Tc T(furopean)Commnit-ie.

transformed and then analysed by means of linear regression (log-normal model). For a better clearness of the model-parameters, a generalised linear model (GLM) was fitted additionally (Austin et al., 2003), using a gamma distribution and a logarithmic link function. Other than log-normal models, gamma models allow to process cost-data in its original scale. To analyse data with both of the models can be viewed as an ad hoc robustness analysis (Wiens, 1999). Coefficients derived from these models may be compared directly and are to be interpreted as the logarithm of the relative change in cost associated with a one-unit change in the predictor variable (or: exponential coefficients provide estimated percentage increases in costs). Goodness-of-fit was assessed by the deviance indicating a good fit in case of low values.

Variables for inclusion into the GLM were selected according to their potential influence on costs of care during the follow-up. For detailed results of the variables used as cost predictors see table 1 or Priebe et al. (2007). The (regression) model selection was done in a stepwise procedure. Thus, p-values of the predictors in the final models should be interpreted in an exploratory manner.

3. Results

Major socio-demographic and disorder related characteristics of the patients are shown in table 1. Utilisation of mental health care services - which provided the basic data for all cost calculations - varied considerably across sites (Table 2). After transforming service utilisation data into cost-of-care data and adjusting for power purchase parities (PPP), there were sizeable inter-site differences in the total cost of mental health care and in most of the service types analysed. Average annual costs of mental health care were lowest in Granada (Spain) and highest in Zurich (Switzerland), where total costs were more than tenfold higher(Fig.1).

Table 1 about here

Table 2 about here

Figure 1 about here

Numerically, the average costs of psychotropic medication was much more constant across sites, whereas the average costs of other services, e.g., hospital or outpatient care, or sheltered accommodation, differed remarkably (see Fig.1). Drug costs claimed a greater proportion of the mental health care costs, the smaller the total cost of care of the respective site was. In Granada, nearly 40% of all costs were accounted for by antipsychotics or other psychotropic drugs, whereas in Zurich this proportion was only 4.6 % (see Fig. 2).

The cost proportions for first- and second-generation antipsychotics were clearly in favour of the latter and more or less constant across sites, with the exception of the Spanish centre, where the proportion spent on second-generation antipsychotics was far lower (see Table 3). The proportion of patients prescribed with second-generation antipsychotics was 61,1 % across all sites. 44,1 % of all patients were treated with first generation antipsychotics and 14 % took both drugs. These proportions differed between centres. Zurich showed had the largest proportion of patients taking second-generation antipsychotics (84.3%) and the smallest first-generation group 27.1 %. In Granada it was the opposite (42.8 % of all patients taking second-generation- and 62.5 % first-generation antipsychotics). The highest share of patients taking both types of agents was identified in Lund (23.6%).

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Table 3 about here

To explore this cost variation further, regression models were fitted separately for two dependent variables:

- total cost of care, and
- medication costs of psychotropic drug intake.

Tables 4 and 5 show the gamma and log normal regression models for total cost of care and medication cost respectively that were calculated due to the skewed distribution of the cost data (see methods section). The tables show only predictors from the total set of variables that proved to be significant at $p \leq 0.05$ during the model selection procedure in at least one model (boldface). All centre-variables were tested against the Zurich centre, which was used as a statistical benchmark due to its high costs.

Table 4 about here

The exponential coefficients *Exp(β)* of the gamma or the log-normal models express the percentage of cost increase or decrease. Thus, the more than tenfold lower mental health care costs in Granada compared to Zurich proved to be significant. Similarly, both models confirm the cost in Groningen as being roughly one third of the cost in Zurich, in London as one quarter, in Lund as two thirds and in Mannheim as approximately half of the costs in Zurich (see Tab.4). Additionally, according to these models, each additional year of age reduces the total mental health care cost of a patient by roughly one percent. But being in sheltered accommodation increases the costs by 71%, whereas a self-earned income or salary cuts the total cost of care by half.

The influence of disorder-related estimates was much lower: each additional negative symptom (PANSS) increases the total care costs by a mere 1.5 %, whereas treatment compliance had a higher influence on costs. However, only the gamma model confirmed this as a significant predictor, while the log-normal model did not.

The intervention from the original RCT (Priebe et al., 2007) proved to have no significant influence on the total care cost: the allocation variable (indicating the experimental or the control group) showed only a trend towards significance in the gamma model ($p \leq 0.10$) and was above the 0.10 level in the log-normal model. Due to the constituent character of this variable for the original RCT, it was retained in the model and shown here, although from a health-economics perspective it is not statistically significant.

Table 5 about here

The two regression models predicting the medication cost (Tab. 5) showed that the influence of the site-variable is considerably less, since the costs of psychopharmacologic drug intake in Lund and Mannheim did not differ significantly from those in Zurich in both statistical models. Only Granada and Groningen showed a drug cost pattern significantly less costly than that of Zurich (shown by both models), whereas the difference with London was confirmed only by the log-normal model.

The association between medication costs and drug compliance at baseline was significant. A change from poor to average, or from average to good compliance was associated

with an overall decrease of drug costs by 29% (confirmed by the gamma model, but not by the log-normal model). Finally, drug costs were associated with needs for care: each additional domain in which the patient thought professional help was needed increased costs by 11% to 22%.

4. Discussion

The study confirms the remarkable differences in the total costs of mental health care for patients with schizophrenia across European countries. This is the case even though the participating patients were homogeneous with respect to diagnosis and other characteristics and all of the relevant countries agree on community mental health care as a basic concept for treating patients with schizophrenia. We found considerably higher inter-site differences than in earlier pan-European projects (Knapp et al. 2002). However, regional cost of care did not exceed the ranges found in earlier national studies (Haro et al., 1998; Salize & Rössler, 1996; Salvador-Carulla et al., 1998; Stant et al., 2003; Vazquez-Polo et al., 2005). Compared to earlier multi-center studies, this study has some methodological advantages which include a long follow-up and recording period of service utilisation (a full 12 months) and the inclusion of detailed medication costs. Different price levels across countries were balanced out by power purchase parities. A weak influence of different salary scales for health workers or other factors could not completely be ruled out, but they are unlikely to account for the huge variation in total costs.

Service provision and consequently service use differed remarkably between the included regions. Although all of the countries practice community care, many reasons may account for the differences across the psychiatric systems: different starting points or specific aims of the national psychiatric reforms, different organisational characteristics of overall health care delivery, different financing structures, different mental health care budgets or economic constraints etc.

Although patients with schizophrenia have a wide range of needs which may vary individually by amount and type, our results suggest that the in principle elastic demand curve of psychiatric care show a clear tendency to follow the regional availability of services. Thus, the cost of care patterns reflect more or less different national mental health care concepts and the characteristic range of services to be found in the participating regions and countries, rather than patient psychopathology or the actual needs for care. Particularly, unmet needs did not have a significant influence on total care costs. If this had been the case, it might have suggested deficient mental health care in regions with low costs,

e.g. in Granada. However, unmet needs were highest in London, and not in the Spanish centre where costs were lowest.

Of course, where services are not available, expenses for them cannot be incurred. However, an absence of specific services does not necessarily mean that treatments such services usually offer are not needed. But when specific services for these needs are not available they tend to be overlooked as a need that requires measures by the professional care system. For example, among other factors, the considerable differences in the availability and use of sheltered accommodation services may be explained by cultural aspects. Families, particularly in southern European countries such as Spain, are traditionally involved – usually at their own expenses - in caring for the chronically mentally ill to a much higher degree than in other European countries. In Middle Europe or Scandinavia, a more pronounced societal trend towards weaker family ties may support the implementation of professional residential services as an essential part of community mental health care.

As a consequence, total costs of care cannot be seen as an indicator for the quality or effectiveness of psychiatric care in a particular region and even less so in cross-border comparisons – at least not on the level of analyses that was done here. For identifying an association between costs and quality of care much better indicators of the global effectiveness of mental health care systems are required than are currently available. Such indicators must cover informal care or any relevant contribution of families and relatives.

Although the effectiveness of the mental health care systems or the commensurability of total care costs cannot finally be decided on this level, the second set of regression analyses (on psychopharmacologic costs) in this study does indicate an association between quality of care and costs. In these regression models centre effects show far less influence on medication costs than they did on the total care costs, despite the considerable proportion that medication costs claim of the total mental health care budgets. In the case of Granada where rehabilitative services or sheltered accommodation are scarce, expenditures for medication rose to nearly 40% of the total expenditure. Medication costs as high as that may reduce the options for prescribing costly second-generation antipsychotics, which accounted for the majority of psychopharmacologic drug costs at all other sites. These issues are worthy of further exploration.

This relative stability of medication costs compared to the total cost of care may have several reasons. First of all, psychopharmacologic drugs represent the backbone of schizophrenia treatment that requires the lowest infrastructure of all psychiatric care modalities. So it would probably be the last of all treatments to be curtailed when cost con-

straints limit mental health care spending. Furthermore, a relatively solid evidence base for the effectiveness of antipsychotic drug treatment is recognised worldwide supporting the homogenisation of drug treatment and the associated costs internationally. Another explanation may be that drug prescription is one of the few sectors of mental health care in which prices are predominantly market driven and far less state regulated than in most other sectors or services where costs may vary according to national health policies, health insurance schemes or public health care spending. Additionally, homogenized price policies of the internationally operating pharmacological companies may contribute to the stability of medication costs.

All in all, the huge overall cost differences as found in this study should be reason enough to stimulate research on the factors that influence service provision, costs and their linkage with outcomes in greater depth and detail (Washburn 2008, Möller 2008, Carpenter & Buchanan 2008). For this purpose, it is essential to build an evidence base for the effectiveness of the service types or treatments for schizophrenic patients in the various care models, and to develop good indicators for their effectiveness on a system level.

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References

Austin, P.C., Ghali, W.A., Tu, J.V., 2000. A comparison of several regression models for analysing cost of CABG surgery. Statistics in Medicine 22, 2799-2815.

Barbui, C., Lintas, C., 2006. Decision models in the evaluation of psychotropic drugs : useful tool or useless toy? Eur J Health Econ 7, 173-175.

Beard, S.M., Maciver, F., Clouth, J., Ruther, E., 2006. A decision model to compare health care costs of olanzapine and risperidone treatment for schizophrenia in Germany. Eur J Health Econ 7, 165-172.

Carpenter, W.T., Buchanan, R.W. 2008. Lessons to take home from CATIE. Psychiatr Serv. 59, 523-525.

Chisholm, D., Knapp, M.R., Knudsen, H.C., Amaddeo, F., Gaite, L., van Wijngaarden. B, 2000. Client Socio-Demographic and Service Receipt Inventory--European Version: development of an instrument for international research. EPSILON Study 5. European Psychiatric Services: Inputs Linked to Outcome Domains and Needs. Br J Psychiatry 39, s28-33.

Davies, A., Vardeva, K., Loze, J.Y., L'italien, G.J., Sennfalt, K., van Baardewijk, M. 2008. Cost-effectiveness of atypical antipsychotics for the management of schizophrenia in the UK. Curr Med Res Opin. 2008 Oct 22. [Epub ahead of print]

Hansen, K., Lancon, C., Toumi, M., 2006. Pharmacoeconomic modelling in schizophrenia. Trap or support for decision makers? Eur J Health Econ 7,19-29.

Haro, J.M., Salvador-Carulla, L., Cabases, J., Madoz, V., Vazquez-Barquero, J.L., 1998. Utilisation of mental health services and costs of patients with schizophrenia in three areas of Spain. Br J Psychiatry 173, 334-340.

Johnson, S., Kuhlmann, R., EPCAT Group, 2000. The European Service Mapping Schedule (ESMS): development of an instrument for the description and classification of mental health services. Acta Psychiatr Scand 405, 14-23.

Jones, P.B., Barnes, T.R., Davies, L., Dunn, G., Lloyd, H., Hayhurst, K.P., Murray, R.M., Markwick, A., Lewis, S.W., 2006. Randomised controlled trial of the effect on Quality of Life of second- vs first-generation antipsychotic drugs in schizophrenia: Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS 1). Arch Gen Psychiatry 63, 1079-1087.

Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull13, 261-276.

Knapp, M., Novick, D., Genkeer, L., Curran, C.M., McDaid, D., SOHO Study Group, 2003 Financing health care in Europe: context for the Schizophrenia Outpatient Health Outcomes Study. Acta Psychiatr Scand 416 (Suppl.), 30-40.

Knapp, M., Chisholm, D., Leese, M., Amaddeo, F., Tansella, M., Schene, A., Thronicroft, G., Vazquez-Barquero, J.L., Knudsen, H.C., Becker, T., and Epsilon Study Group, 2002. Comparing pattrerns and costs of schizophrenia care in five European Countries: the Epsilon Study. Acta Psychiatrica Scandinavica 105, 42-54.

Möller, H.J. 2008. Do effectiveness ("real world") studies on antipsychotics tell us the real truth? .Eur Arch Psychiatry Clin Neurosci 258, 257-270.

Nguyen, T.D., Attkisson, C.C., Stegner, B.L., 1983. Assessment of patient satisfaction: development and refinement of a service evaluation questionnaire. Eval Program Plann 6, 299-313.

Priebe, S., Huxley, P., Knight, S., Evans, S., 1999. Application and results of the Manchester Short Assessment of Quality of Life (MANSA). Int J Soc Psychiatry 45, 7-12.

Priebe, S., McCabe, R., Bullenkamp, J., Hansson, L., Lauber, C., Martinez-Leal, R., Rössler, W., Salize, H.J., Svensson, B., Torres-Gonzales, F., van den Brink, R., Wiersma, D., Wright, D.J., 2007. Structured patient-clinician communication and one-year outcome in community mental health care: A cluster randomised controlled trial. British Journal of Psychiatry191, 420-426.

Priebe, S., McCabe, R., Bullenkamp, J., Hansson, L., Rössler, W., Torres-Gonzales, F., Wiersma, D., 2002. The impact of routine outcome measurement on treatment processes in community mental health care: approach and methods of the MECCA study. Epidemiol Psichiatr Soc 11, 198-205.

Rosenheck, R.A., Leslie, D.L., Sindelar, J., Miller, E.A., Lin, H., Stroup, T.S., McEvoy, J., Davis, S.M., Keefe, R.S., Swartz, M., Perkins, D.O., Hsiao, J.K., Lieberman, J., CATIE Study Investigators, 2006. Cost-effectiveness of second-generation antipsychotics and perphenazine in a randomised trial of treatment for chronic schizophrenia. Am J Psychiatry 163, 2080-2089.

Rosenheck, R.A., 2006. Outcomes, costs, and policy caution. A commentary on: the Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS 1). Arch Gen Psychiatry 63, 1074-1076.

Salize, H.J., Rössler, W., 1996. How Expensive is the Comprehensive Care of Schizophrenic Patients in the Community - A Cost Evaluation from a German Catchment Area. British Journal of Psychiatry 169, 42-48.

Salvador-Carulla, L., Haro, J.M., Cabases, J., Madoz, V., Sacristan, J.A., Vazquez-Barquero, J.L., 1999. Service utilization and costs of first-onset schizophrenia in two widely differing health service areas in North-East Spain. PSICOST Group. Acta Psychiatr Scand 100, 335-343.

Slade, M., Phelan, M., Thornicroft, G., Parkman, S., 1996. The Camberwell Assessment of Need (CAN): comparison of assessments by staff and patients of the needs of the severely mentally ill. Soc Psych Psychiatr Epidemiol 31, 109-113.

Stant, A.D., TenVergert, E.M., Groen, H., Jenner, J.A., Nienhuis, F.J., van de Willige, G., Wiersma, D., 2003. Cost-effectiveness of the HIT programme in patients with schizophrenia and persistent auditory hallucinations. Acta Psychiatr Scand 107, 361-368.

Vazquez-Polo, F.J., Negrin, M., Cabases, J.M., Sanchez, E., Haro, J.M., Salvador-Carulla, L., 2005. An analysis of the costs of treating schizophrenia in Spain: a hierarchical Bayesian approach. J Ment Health Policy Econ 8,153-165.

Washburn, C.F. Jr. 2008. Problems with CATIE. Phase 1: Looking back--what the clinician needs to know. Conn Med 72, 223-226.

Wiens, B.L., 1999. When log-normal and gamma models give different results: A case study. The American Statistician 53, 89-93.

Windmeijer, F., Kontodimas, S., Knapp, M., Brown, J., Haro, J.M., 2006. Methodological approach for assessing the cost-effectiveness of treatments using longitudinal observational data: the SOHO study. Int J Technol Assess Health Care 22, 460-468.

Zhu, B., Scher-Svanum, H., Faries, D.E., Correll, C.U., Kane, J.M. 2008. Cost of antipsychotic polypharmacy in the treatment of schizophrenia. BMC.Psychiatry 8: 19.
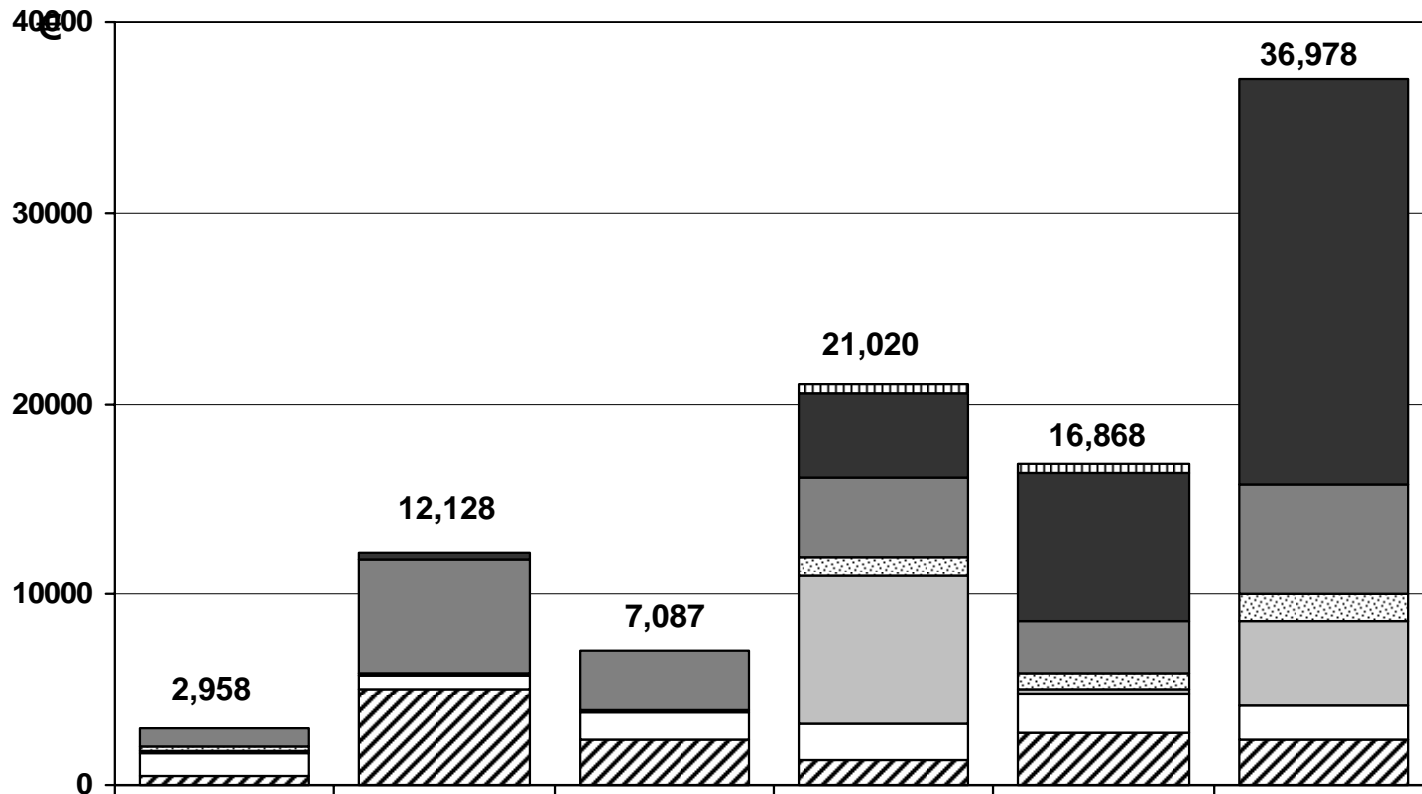
	Granada	Groningen	London	Lund	Mannheim	Zürich
⊞ other	16	0	0	491	532	46
■ sheltered acccommodation	0	314	103	4395	7713	21174
▨ CMHC / day care	920	5984	3091	4126	2740	5804
▨ outpatient/ outreach services	226	57	23	1032	861	1400
▨ outpatient dep./day hospital	156	26	0	7703	285	4484
▢ psychotropic medication	1181	768	1484	1947	2019	1695
▨ inpatient hospital care	459	4979	2387	1278	2715	2425

	medication		hospital		outpatient		sheltered accomodation		others

39.9 %   **6.3 %**   **20.9 %**   **9.3 %**   **12 %**   **4.6 %**
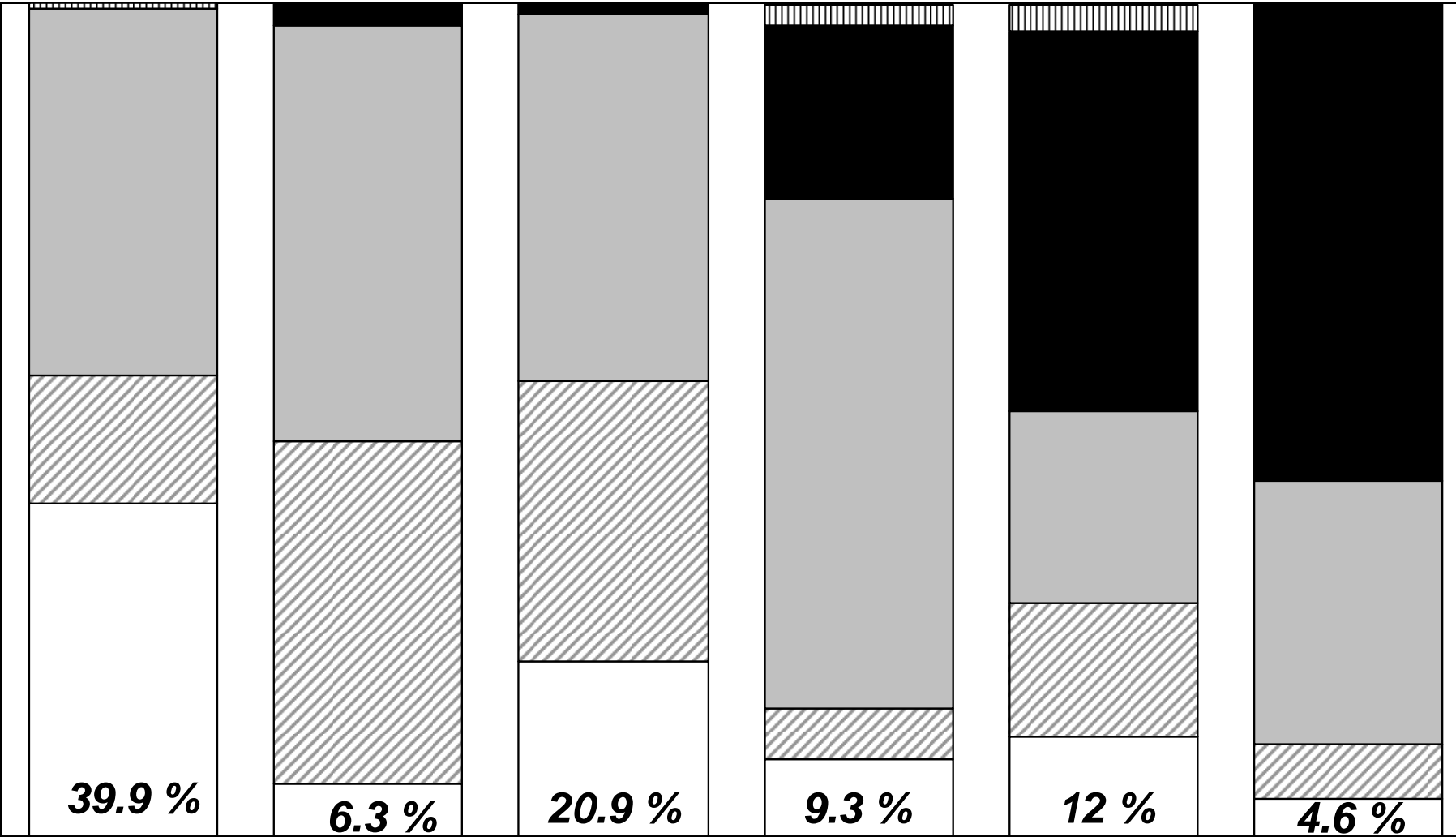
Granada   **Groningen**   **London**   **Lund**   **Mannheim**   **Zurich**

Table 1 **Baseline socio-demographic characteristics of patients, means (standard deviation SD) or proportions (%)**
(Mansa: Manchester Short Assessment of Quality of Life, CSQ: Client Satisfaction Questionnaire, Cansas: Camberwell Assessment of Need Short Appraisal Schedule, PANSS: Positive and Negative Syndrome Scale)

	Mean (SD) or Proportion
Patients (n)	422
Mean Age (years)	42.3 (11.3)
Gender (% female)	31.8 %
Marital status (% single)	70.8 %
Unemployed (%)	36.7 %
Employed (incl. Sheltered Work)	29.4 %
Diagnosis	
Undifferentiated Schizophrenia	35.1 %
Paranoid Schizophrenia	30.1 %
Other Schizophrenia (Schizoaffective, Delusional etc.)	18.4 %
Other Non-Organic Psychotic Disorder	16.4 %
Length of illness (years)	16,0 (10.1)
Number of hospital admissions	5.2 (7.1)
Quality of Life (MANSA)	4.7 (0.8)
Satisfaction with treatment (CSQ)	25.7 (4.2)
Unmet needs (CANSAS)	2.7 (2.8)
PANSS Subscales	
Positive	14.8 (5.7)
Negative	16.6 (6.7)
General	32.4 (9.6)

Table 2 **Mental health care service utilization across sites (average frequency of contacts with or days spent in service per patient during the 12-month follow-up) (CMHC: Community Mental Health Centre)**

	Granada	Groningen	London	Lund	Mannheim	Zurich
Sample size	56	94	81	55	66	70
Psychiatric Hospital	0.9	18.1	7.8	2.8	13.4	6.2
Emergency/Crisis Ward	0.1	0	0	0.1	0.1	0.2
General Medical Wards	0	0	0	0	0	0
Other Inpatient Services	0	0	0	0.9	0	0
Total hospital days	*0.88*	*18.17*	*7.78*	*3.78*	*13.38*	*6.27*
Outpatient Visits	0	0.2	0	42.3	0.4	19.3
Day/Night Hospital	1.4	0	0	12.1	2.1	1.9
Other outpatient services	0	0.1	0	3.9	0.2	0.6
CMHC	7.4	32.4	24.2	15	5	0.6
Day Care	25.9	30	6.1	12.4	56.5	1.6
Sheltered Workshop	4.6	3.6	1.7	8.7	53.8	107.1
Sheltered Education Service	0.1	0.5	0.7	5.9	4.6	1.2
Other day services	0	0	0	0.1	21.3	14.1
Psychiatrists	0	0	0	0.7	13	3.3
Psychologists	0	0	0	2.1	2.4	1.1
Primary Care Physicians	3.7	0.3	0	0.4	1.8	0.9
Psychiatric Nurses	0	0	0	1.2	1.9	0.1
Social Worker	0	0	0	0.2	0.8	0.3
Occupational Therapists	0	0	0	1.4	2.1	1.9
District Nurses	0	0	0	0.3	2.9	6.9
Home Help	0	0.6	1.1	7.2	1	2.4
Other Services	0	0	0	0.3	2	8.2
Overnight 24h staffed	0	0	0.7	13.3	2.8	26.6
Overnight not 24h staffed	0	2.9	0	13.0	276.1	135.4
Overnight not staffed	0	0	0	0	0	12.9
Other home	0	0	0	0	0	15.4

Tab. 3 **Cost proportions for first- and second-generation antipsychotics across sites (100% = average annual medication cost per patient)**

	Granada	Groningen	London	Lund	Mannheim	Zurich
% second generation antipsychotics	49.4 %	80.0 %	80.5 %	64.8 %	81.3 %	74.5 %
% first generation antipsychotics	38.9 %	9.7 %	8.7 %	8.6 %	10.9 %	5.5 %
% other psychotropic drugs	11.8 %	10.3 %	10.8 %	26.6 %	7.8 %	20.0 %
Total medication cost (100%)	1 181.27	767.98	1 483.70	1 947.08	2 019.46	1 695.40

Tab. 4 **Regression model for predictors of total costs of mental health care** (coefficients in boldface are significant at p≤0.05)
(PANSS: Positive and Negative Syndrome Scale)

variable	gamma model		log-normal model	
	β	$Exp(\beta)$	β	$Exp(\beta)$
Centre 1 (Granada) [1]	**- 2.3228**	**0.0980**	**- 2.3974**	**0.0912**
Centre 2 (Groningen) [1]	**- 0.9674**	**0.3801**	**- 1.1207**	**0.3261**
Centre 3 (London) [1]	**- 1.4285**	**0.2397**	**- 1.5398**	**0.2144**
Centre 4 (Lund) [1]	**- 0.3952**	**0.6735**	**- 0.4260**	**0.6531**
Centre 5 (Mannheim) [1]	**- 0.6985**	**0.4973**	**- 0.5728**	**0.5639**
Age	**- 0.0112**	**0.9888**	**- 0.0099**	**0.9902**
Living situation	**0.5376**	**1.7119**	**0.5488**	**1.7312**
Main income source	**- 0.8411**	**0.4312**	**- 0.7366**	**0.4788**
Panss negative score follow-up	**0.0141**	**1.0142**	**0.0160**	**1.0161**
Treatment adherence baseline	**0.1955**	**1.2159**	0.0568	1.0584
allocation to experimental group	0.1545	1.1671	0.1373	1.1472
Deviance	282.62		290.09	

[1] Compared against Centre 6 (Zurich, Switzerland)

Table 5 **Regression model for predictors of average medication costs** (coefficients in bold are significant at p≤0.05)

Variable	gamma model		log-normal model	
	β	$Exp(\beta)$	β	$Exp(\beta)$
Centre 1 (Granada) [1]	**- 0.3962**	**0.6792**	**- 0.6287**	**0.5333**
Centre 2 (Groningen) [1]	**- 0.7299**	**0.4820**	**- 1.4049**	**0.2454**
Centre 3 (London) [1]	- 0.1168	0.8900	**- 0.4969**	**0.6084**
Centre 4 (Lund) [1]	0.0792	1.0824	- 0.2216	1.8012
Centre 5 (Mannheim) [1]	0.2133	1.2378	0.0698	1.0723
Age	**- 0.0121**	**0.9880**	- 0.0126	0.9875
No. of domains help needed	**- 0.1053**	**1.1110**	**- 0.1990**	**1.2202**
Drug compliance baseline	- 0.0798	0.9233	**- 0.3360**	**0.7146**
Deviance	526.34		937.05	

[1] Compared against Centre 6 (Zurich, Switzerland)