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Original article

The economic burden of schizophrenia in Germany: A population-based retrospective cohort study using genetic matching

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ABSTRACT

Objective: Prior studies to determine the economic consequences of schizophrenia have largely been undertaken in clinical settings with a small number of cases and have been unable to analyze effects across different age cohorts. The aim of this study is to investigate the burden of schizophrenia in Germany.

Methods: Costs, service utilization, and premature mortality attributable to schizophrenia were estimated for the year 2008 using a retrospective matched cohort design. Therefore, 26,977 control subjects as well as 9411 individuals with a confirmed diagnosis of schizophrenia were drawn from a sickness fund claims database. To reduce conditional bias, the non-parametric genetic matching method was employed.

Results: The final study population comprised 8224 matched pairs. The annual cost attributable to schizophrenia was €11,304 per patient from the payers' perspective and €20,609 from the societal perspective with substantial variations among age groups: direct medical expenses were highest among patients aged > 65 years, whereas younger individuals (< 25 years) incurred the greatest non-medical costs. The annual burden of schizophrenia from the perspective of German society ranges between €9.63 billion and €13.52 billion.

Conclusion: There are considerable differences in the distribution of costs and service utilization for schizophrenia. Because schizophrenia is characterized by an early age of onset and a long duration, research efforts should be targeted at particular populations to obtain the most beneficial outcomes, both clinically and economically.

1. Introduction

Schizophrenia is one of the most burdensome mental illnesses. It follows a chronic relapsing course and is characterized by cognitive and emotional deficits, functional impairment, and social withdrawal in a large number of patients [73]. Depending on the source of information between 0.57% [50] and 0.80% [75] of the German population, i.e., approximately 500,000 persons, are estimated to suffer from schizophrenia. Incidence rates decrease at older ages, and men are slightly more likely to be affected than women (1.4:1). Because of its early onset, the average duration that an affected person lives with the disease is 30 years [74] and most patients require intensive medical treatment during that time.

Previous analyses have found it difficult to capture the economic burden of schizophrenia as a whole. Some studies concentrate on the payers' perspective, and thus on a narrow subset of cost categories, e.g., the direct medical costs of the disease [25,62,34,66,64,27,76]. Most studies have been criticized for their small and selective samples [65] as well as their methodological shortcomings, as described by Kilian et al. [35] and, more generally, by Akobundu et al. [3] or Larg and Moss [43]. At the time of writing, none of the available studies included a matched control group to appropriately isolate schizophrenia-attributable costs. Only one study [53] attempted to examine the economic consequences of schizophrenia on a national level. This situation seems entirely unsatisfactory, given that cost-of-illness (COI) studies are frequently used to legitimize cost-reduction efforts directed towards particular caregiving entities, population groups, or service levels in health care.

Over the past decades, there have been major shifts in the treatment of schizophrenia as pharmacotherapy and disease management programs have evolved. This has stimulated a debate on the cost-effectiveness of therapeutic strategies and in particular of the (costly) second-generation neuroleptic drugs, while raising decision-makers' and service providers' expectations to reduce the

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cost of institutional care, and thus the burden of schizophrenia in general. Now that economic evidence has become available in the form of claims data that reflect routine care conditions, it is possible to assess whether this result has actually occurred. This study provides a comprehensive analysis of the economic resources dedicated to schizophrenia care. Because the outcomes were expected to diverge substantially depending on patients' ages, one of the main aims was to investigate the burden of disease across different age cohorts.

2. Materials and methods

2.1. Study design and population

To determine the economic burden of the disease from both the payers' perspective and the societal perspective, a non-experimental retrospective cohort design was adopted. The data for the analysis were obtained from a large sickness fund (Techniker Krankenkasse), which provides coverage for 7.9 million German residents who have statutory health insurance (SHI). Since roughly 87% of the German population are enrolled in the SHI system [9], the Techniker Krankenkasse represents 11.4% of them. The data included longitudinal micro-level information on in- and outpatient service utilization and costs, pharmacy claims, frequency and duration of sick-leave, retirement status, and demographic information. This was augmented by data from the Federal Statistical Office. For the main analysis, 9411 insured individuals with a history of schizophrenia, i.e., any hospitalization between 2005 and 2008 coded with ICD-10-GM (International Classification of Diseases, Tenth Revision, German Modification) F20.'x' were selected. A random sample of 26,977 individuals without schizophrenia, stratified by year of birth and sex, was drawn from the same database and served as a basis for the control cohort.

The causal effect of schizophrenia on costs, service utilization, and mortality was isolated using the 'potential outcomes' framework [59,29]. This approach entails finding and comparing matched pairs that are virtually identical except for the condition of interest (i.e., schizophrenia, in the present study). The primary study outcomes 'direct and indirect disease costs', 'service utilization', and 'premature mortality' were measured in the year 2008. A bottom-up, prevalence-based approach was chosen to reflect resource consumption for age-specific subgroups [49]. When possible, the categories of resource consumption were based on national standardized taxonomies [33]. Table 1 contains a breakdown of the various cost categories and the evaluation perspectives (sickness fund perspective and societal perspective) that were used in the analysis.

Table 1
Cost categories used in the study.

Cost category	Perspective	
	Sickness fund	Societal
Direct medical costs		
Outpatient treatment	+/+	+/+[a]
Drugs	+/+	+/+[a]
Medicinal substances (remedies)	+/+	+/+
Devices and medical assistive equipment	+/+	+/+
Inpatient treatment	+/+	+/+[a]
Rehabilitation	+/+[b]	+/+[b]
Medical services (nursing care at home)	+/+[b]	+/+[b]
Direct non-medical costs		
Administration	+/+	+/+
Sick-leave compensation	+/+	−/−
Investments	−/−	+/+
Travel costs	+/+[b]	+/○ [b]
Other non-medical services	+/+[b]	+/○ [b]
Patient time (loss of leisure time)	−/−	+/−
Informal family care (loss of leisure time)	−/−	+/+
Indirect costs		
Reduced work productivity	−/−	+/−
Incapacity for work	−/−	+/+
Occupational disability	−/−	+/+
Premature death	−/−	+/+

Adapted from IQWiG 2009.
+ = yes; − = no; ○ = partial. First sign indicates whether the respective element is relevant within the given perspective, while the second sign indicates whether the element was actually available for the analysis.
[a] Including consultation fee/co-payment.
[b] Including only costs that are reimbursed by the sickness fund.

2.2. Matching

In clinical studies, randomization is applied to eliminate differences in baseline characteristics between the treatment groups [70]. By contrast, random allocation to treatment is absent in observational studies [11]. As a consequence, schizophrenia and control subjects from this study's claims database may differ not only with respect to the condition of interest but also with respect to baseline demography, comorbidities, and/or other prognostic attributes. For example, the schizophrenia group had a higher proportion of men (54.3%) than the controls (49.7%) (t-test $P < 0.001$). These differences partly reflect underlying imbalances in patient mix, which may lead to selection bias and potentially invalid results. To resolve the problem, each schizophrenia patient was matched to its most similar control based on predefined observable characteristics [60]. This was done using the relatively novel genetic matching (GM) approach, which was first described by Sekhon and Mebane [69] and was recently applied in health care research [24,68,41]. The aim of GM, as of any matching approach, is to maximize the comparability of study cohorts with respect to potential confounders. It was shown that confounder balance can be improved by combining matching methods that rely on a unidimensional score (i.e., propensity score [PS] matching), and matching on the individual covariates [58]. For this purpose, GM uses an algorithm to automatically determine weights for each covariate. If desired, a propensity score may be included as an additional matching variable. The actual selection of matched pairs is then performed by minimizing the multivariate distance between individuals based on the weighted covariates, and this procedure is repeated until the best possible confounder balance in the overall sample is achieved [15]. Because GM is a multivariate method, it is less sensitive to misspecifications of the PS model as compared with univariate PS matching. Diamond and Sekhon [15] also demonstrate that GM performs well in adjusting for key confounders, even when baseline differences are large or have skewed distributions. The final effect sizes (the so-called average treatment effects on the treated, ATT, [32]) were obtained by subtracting mean outcomes in the matched control cohort from mean outcomes in the schizophrenia cohort.

Prior to the actual matching, one has to determine patient baseline characteristics that influence the outcome of interest. The present study considered demographic characteristics and comorbidity to be potential confounders. Baseline variables were measured in 2007. The presence of comorbidities was assessed using well-established binary indicators for predefined clinical conditions. They were extracted from the dataset based on 27 diagnostic classification groups [17] and 28 drug prescription-based classification groups [42], both of which have been proposed to control for confounding in studies using claims data [18]. Four diagnostic clusters (alcohol abuse, drug abuse, psychoses, and depression) and four drug prescription clusters (depression, psychotic illness, bipolar disorders, anxiety and tension) were