Size of burden of schizophrenia and psychotic disorders

Wulf Rösslera,*, Hans Joachim Salize b, Jim van Os c, Anita Riecher-Rössler d

aPsychiatric University Hospital, Militärstrasse 8, CH-8021 Zurich, Switzerland
bCentral Institute of Mental Health, Mannheim, D, Switzerland
cDepartment of Psychiatry and Neuropsychology, Maastricht University, NL, Switzerland
dUniversity Psychiatric Outpatient Department, University Hospital Basel, CH, Switzerland

Abstract

Schizophrenia is a severe mental disorder characterised by fundamental disturbances in thinking, perception and emotions. More than 100 years of research have not been able to fully resolve the puzzle that schizophrenia represents. Even if schizophrenia is not a very frequent disease, it is among the most burdensome and costly illnesses worldwide. It usually starts in young adulthood. Life expectancy is reduced by approximately 10 years, mostly as a consequence of suicide. Even if the course of the illness today is considered more favourable than it was originally described, it is still only a minority of those affected, who fully recover. The cumulative lifetime risk for men and women is similar, although it is higher for men in the age group younger than 40 years. According to the Global Burden of Disease Study, schizophrenia causes a high degree of disability, which accounts for 1.1% of the total DALYs (disability-adjusted life years) and 2.8% of YLDs (years lived with disability). In the World Health Report [The WHO World Health Report: new understanding, new hope, 2001. Geneva], schizophrenia is listed as the 8th leading cause of DALYs worldwide in the age group 15–44 years. In addition to the direct burden, there is considerable burden on the relatives who care for the sufferers. The treatment goals for the moment are to identify the illness as early as possible, treat the symptoms, provide skills to patients and their families, maintain the improvement over a period of time, prevent relapses and reintegrate the ill persons into the community so that they can lead as normal a life as possible.

Keywords: Psychosis; Schizophrenia; Epidemiology; Burden; Costs; Gender differences; Early detection

1. Introduction

Schizophrenia and psychotic disorders are combined in the chapter F2 of the International Classification of Diseases (ICD-10). It is a heterogeneous category, mainly merged for practical reasons. The most frequent and most important illness group is schizophrenia. This illness entity was first described by Emil Kraepelin (1896). He separated schizophrenia from manic-depressive illness, initially naming the syndrome “Dementia praecox”. The term schizophrenia, not introduced until 1911, was coined by Eugen Bleuler (1911).

More than 100 years of research have not been able to fully resolve the puzzle that schizophrenia represents, but much progress has been booked over the last two decades. Schizophrenia behaves epidemiologically like other complex disease phenotypes, such as diabetes and cardiovascular disease, in that the disease tends to cluster in families; yet genetic factors appear to be neither necessary nor sufficient to produce illness onset (Murray et al., 2003). Thus, the causation of schizophrenia involves multiple interactions between genes and environment over the life course (van Os and Marcelis, 1998)–probably often starting as early as fetal life (Susser et al., 1999)–and leaving traces in the early social, motor and cognitive development of children later destined to develop schizophrenia (Jones et al., 1994). Four-fifths of the differences in liability to schizophrenia are...
attributable to genes and the first probable risk genes have been identified, although their function remains unclear (Harrison and Owen, 2003). Their effects are small and many may be involved. They are likely to interact with environmental exposures that impact on the individual over the life course, such as fetal hypoxia (Cannon et al., 2002), the proxy environmental risk factor: season of birth (Mortensen et al., 1999), adverse rearing environments (Tienari et al., 2004), the stresses of urban life during upbringing (van Os et al., 2003, Spauwen et al., 2004), cannabis use (Verdoux et al., 2003), stress in daily life (Myin-Germeys et al., 2001) and a minority position (Hutchinson et al., 1996). The causes of schizophrenia impact on brain development, as evidenced by a small reduction in the volume of grey matter (Wright et al., 2000) that appears to progress over time, and may be linked to social deterioration, use of medication or factors intrinsic to the disease itself (Cahn et al., 2002, Ho et al., 2003a,b).

2. Incidence and prevalence of schizophrenia

Schizophrenia occurs worldwide. Incidence seems to be very similar worldwide, at least if schizophrenia is narrowly defined, i.e. with a nuclear schizophrenic syndrome consisting mainly of first-rank systems at onset (Sartorius et al., 1986; Jablensky et al., 1992). With a wider disease concept, reported rates vary between and within countries. From the lowest (0.3 per 1000) to the highest (22 per 1000) (Torrey, 1987; Hovatta et al., 1997) prevalence rates, there are more than 50-fold variations, with differences being due partly to differing observation times and methodology, and partly to true differences (see Wittchen and Jacobi, 2005). Lifetime prevalence has been reported in the range of 0.5% to 1.6%; i.e. out of 100 individuals, about one will experience a schizophrenic episode in his lifetime (Jablensky, 1995).

Concerning European prevalence rates, a recent German survey (Wittchen et al., 2000; Jacobi et al., 2004) names a 12-month prevalence rate of 26 cases and a lifetime prevalence of 45 cases for having any psychotic syndrome per 1000 population of 18–65 years. Psychotic syndromes as defined in this study include schizophrenia, schizoaffective, delusional disorders as well as psychotic syndromes occurring in the course of depressive and bipolar disorders. The Munich Follow-up Study (Wittchen et al., 1992) found a lifetime prevalence rate of 7 per 1000 for schizophrenia and schizophreniform disorder. In a Dutch survey, the lifetime prevalence rate for schizophrenia was 4 and the 12-month prevalence rate 2 per 1000 (Bijl et al., 1998). Jenkins et al. (1997) found in a household survey in Great Britain a 1-year prevalence of 4 per 1000 (including psychotic disorders according to ICD-10 chapters F20 and F30).

As regards incidence rates, the “Determinants of Outcome of Severe Mental Disorders”, DOS Study by the WHO was one of the first methodologically sound, representative studies on worldwide incidence rates for schizophrenia (Jablensky et al., 1992; Sartorius et al., 1986). Departing from a narrow schizophrenia concept, between 0.7 and 1.4 cases per 10,000 population were found to arise in 1 year. Based on a wider concept, the incidence was 1.6 to 4.2 cases per 10,000 population and per year. These figures correspond well to those found in the German ABC Study, which was one of the first representative European studies on all first-admitted patients from a defined catchment area. It found incidence rates of 1.7 per 10,000 and year for ICD-schizophrenia only and 1.9 per 10,000 and year using a wider disease concept that also included paranoid disorders (Riecher-Rössler et al., 1997).

Independent of variations in incidence rates, recent research suggests that the incidence of schizophrenia may be declining. Such a decline, for example, was reported by Suvisaari et al. (1999). Based on the Finnish population register between 1954 and 1965, they found for each successive cohort a decline from 0.79 to 0.53 per thousand among males and from 0.58 to 0.41 per 1000 among females. One of the reasons might be the conceptual narrowing of schizophrenia, evidence for which was provided in a recent study (Allardyce et al., 2000).

On the other hand, epidemiological surveys report prevalence rates of hallucinatory and delusional experiences in the general population of between 10% and 15% (Johns and van Os, 2001). These symptoms, although not yet of clinical relevance or associated with substance abuse, obviously do have strong predictive power for the onset of clinical psychotic disorders later in life (Poulton et al., 2000).

3. Course

In his first descriptions, Kraepelin expressed a very pessimistic view of the course of the illness. He was of the opinion that the illness follows a path of continuous progression with persistent and serious symptoms in over 70% of the cases. Today, we know that this poor course was mainly due to Kraepelin’s selected samples of long-term hospitalised patients living in the deprived environment of isolated asylums. Since then, numerous studies have shown a better course. Hegarty et al. (1994) identified a total of 821 studies on the course of schizophrenia that were carried out between 1895 and 1992: Of these, 320 satisfied methodological standards. In this meta-analysis, 40.2% of the patients were considered to have improved after follow-ups averaging 5.6 years. The proportion of patients who improved increased significantly after mid-century. In the 1980s, the outcome seemed to deteriorate again. However, this finding was probably mainly an artefact, reflecting the re-emergence of narrow diagnostic concepts.

The largest studies on the course of schizophrenia have been coordinated by the WHO. Within the framework of the so-called “Disability Study”, An der Heiden et al. (1995) conducted a 14-year follow-up assessment of the German sample in Mannheim. About one third of the patients still showed delusions or hallucinations. Almost the same
number suffered from psychological impairments and two thirds were socially disabled.

The Nottingham sub-sample of the WHO-“DOS Study” (see above) has been followed-up over 14 years. Of that sample, 18% never relapsed and 25% were never readmitted. However, 33% of the cohort experienced psychotic symptoms almost continuously. At the 13-year follow-up, as many as 44% of the patients were found to have recovered or be only mildly impaired (Mason et al., 1996).

Apart from some well-known American studies, e.g. the “Iowa 500 Study” (Tsuang et al., 1979), the “Chestnut Lodge Study” (McGlashan, 1984a,b) or the “Vermont Study” (Harding et al., 1987a,b), there are only a few European studies that have provided prospective and standardised data on representative samples of first-admitted patients.

One of these is the “Buckinghamshire Study” by Shepherd et al. (1989). Twenty-two percent of his patients remained symptom-free over 5 years following the first admission. Thirty-five percent developed further discrete episodes, but were free of psychotic symptoms between episodes. Eight percent had persistent florid symptoms with one or more exacerbations, and suffered from stable residual psychopathology between episodes. Thirty-five percent showed the same florid picture, with increasing impairment after each episode.

It has been repeatedly demonstrated that schizophrenia follows a more severe course in industrialised countries like Europe, as opposed to developing countries (Thara and Eaton, 1996). For example, in the WHO-DOS Study, the proportion of patients showing full remission at 2 years was 63% in developing countries, compared to 37% in developed countries (Jablensky et al., 1992). Though attempts have been made to explain this better outcome on the basis of stronger family support and fewer demands on the patients, the exact reasons for these differences are not clear.

Social functioning is another indicator of the course of illness. With respect to that indicator, more than one third of the patients of the “Determinants of Outcome Study” showed no sign of disability during at least three quarters of the observation period and only less than one third suffered more or less severe impairments during the entire 2 years. Shepherd et al. (1989) rated social impairment after 5 years. Of their patients, 45% showed only minimal impairment, 43% mild to moderate and 12% severe impairment. In their ability to work, 24% of patients were mildly to moderately impaired and 16% impaired. Almost half of the patients were mildly to moderately disturbed in their leisure and social skills, and 15% severely disturbed. Finally, in family relationships, there were mild to moderate problems for 36% and severe problems for 14% of the patients. In the “ABC Study” (Häfner et al., 1995, 1998), it was shown that these impairments often already occur in the early preclinical course of the disease. As compared with their peers, these very often young patients frequently lag behind in their social development from the start.

The course of the illness has been found to be better in women (also see below), in patients who had an acute, stress-related onset of their illness, low levels of negative symptoms, higher social class, better premorbid social development and no evidence of cannabis use (Kelly et al., 2001).

4. Burden

The burden of schizophrenia is large and multifaceted. Headmost, there are the direct costs of providing care for individuals with schizophrenia. The indirect costs encompass the loss of productivity through impairments, disability and premature death, burden on caregivers, as well as some legal problems—including violence.

One specific aspect of burden is the health burden, which has preferably been measured in national and international health statistics in terms of incidence/prevalence and mortality. While these indicators are well suited for acute diseases that either cause death or result in full recovery, their use for chronic and disabling diseases, like schizophrenia is limited. One way to account for the chronicity of disorders and the disability they cause is the Global Burden of Disease (GBD) methodology. GBD introduced a new metric called disability-adjusted life year (DALY) to quantify the burden of diseases. DALY combines information on the impact of mortality (years of life lost because of premature death = YLL) and disability (years lived with disability = YLD). One DALY can be thought as one lost year of “healthy” life. According to the Global Burden of Disease Study (Murray and Lopez, 1996, 1997), schizophrenia causes a high degree of disability that accounts for 1.1% of the total DALYs and 2.8% of YLDs. In the World Health Report (2001), schizophrenia is listed as 8th leading causes of disability-adjusted life years worldwide in the age group 15–44.

However, there are concerns about the universality of the disability weights used. Therefore, Üstün et al. (1999) undertook a study to investigate the stability of such weighting in different countries and informant groups. In their 14-country study on disability associated with physical and mental conditions, active psychosis was ranked the third most disabling condition, higher than paraplegia and blindness, by the general population (Üstün et al., 1999).

A further study, based on the Global Burden of Disease Study, assessed the degree of dependency, i.e. the need for daily assistance from another person in carrying out health, domestic or personal tasks. Again, active psychosis was ranked in the highest disability class, requiring daily care (Harwood et al., 2004).

5. Mortality

Globally, schizophrenia reduces an affected individual’s life span by on average 10 years (World Health Report, 2001).
Mortensen and Juel (1993) analysed case-register data of 9156 patients with schizophrenia. They found that, compared to the age-standardised general population, the relative mortality risk of male schizophrenia patients was increased 4.7-fold and that of female patients 2.3-fold. This increased mortality seems to be due mainly to suicide. A recent study showed that 30% of patients diagnosed with schizophrenia had attempted suicide at least once during their lifetime (Radomsky et al., 1999). About 10% of the patients die by suicide (Caldwell and Gottesman, 1990).

Hiroeh et al. (2001) also recorded an increased risk of dying by homicide in men with schizophrenia. Furthermore, individuals with schizophrenia show an increased morbidity due to natural causes (Hewer et al., 1995, Hewer and Rössler, 1997), which certainly also contributes to their increased mortality.

6. Burden on patients, families and communities

Schizophrenia has a large impact, not only on individuals, but also on families and communities. Individuals suffer primarily from the distressing symptoms of disorders. They also lack self-esteem because they are unable to participate in work and leisure activities, often not only as a result of disability, but also because of the stigma and discrimination. Not quite unjustified, they additionally worry about being a burden for others.

The burden on families ranges from emotional reactions to the illness, the stress of coping with disturbed behaviour, the disruption of household routine, the stigma they too are confronted with and the restriction of social activities, to economic difficulties. Restriction of involuntary hospital admission and reduced lengths of hospital stay can further increase the burden on relatives. In a study by Lauber et al. (2003), the most important predictor of the burden on relatives was the distress and changes in the relationship between caregiver and the affected individual that occur during acute illness. Threats, nuisances, time spent with the affected one and restricted social life and leisure activities were additional predictors. Despite their burden, relatives do not complain much, although they sometimes receive little support, advice or information from the professionals engaged in treating the respective patient (Fadden et al., 1987).

If one converts relatives’ time and effort of caring for their affected ones during acute illness into euro, the sum of money amounts roughly to the expenses of inpatient treatment (Lauber et al., in press). In a study conducted by Magliano et al. (2002), (reduced) family burden was associated with professional and social network support received by the family. Thus, professional and social network support represents a crucial resource to reduce family burden in schizophrenia. Mental-health services should therefore aim to assist key caregivers for people with chronic schizophrenia to manage stress, whether or not the patient lives in the same household as the caregiver (Laidlaw et al., 2002).

In addition to the direct burden, hidden burdens have to be taken into account. Based on data from the U.S. National Health Survey, Gallagher and Mechanic (1996) compared respondents living with the mentally ill with randomly selected respondents not living with anyone mentally ill concerning health outcomes. They found that sharing a household with someone who is mentally ill is associated with poorer self-reported physical health, increased reporting of activity limitation, increased service utilisation and other negative consequences.

The social and emotional environment within the family has been found to correlate with relapses in schizophrenia. This led to research on the cause of this phenomenon. Most studies have used the concept of “expressed emotions”. It describes the attitude and behaviour of family members towards the individuals with schizophrenia, especially critical comments, hostility, lack of warmth or emotional over-involvement. A large number of studies have demonstrated in the meantime that expressed emotions can predict the course of schizophrenia, including relapses (Butzlaff and Hooley, 1998). Some studies have shown that a combination of regular medication, family education and family support can reduce the rate of relapses from 50% to less than 10% (Fig. 1).

7. Legal problems

It is a longstanding public belief that schizophrenia is associated with an increased risk of violence. In fact, Angermeyer (2000), in a meta-analysis of studies from the 1990s, found that there is an increased risk of violence in terms of odds ratios between 4 and 8 predominantly for men with schizophrenia. This risk is even more elevated if there is comorbid substance abuse. Nevertheless, there is only a negligible—but possibly growing—proportion (Munk-Jørgensen, 1999) of community violence that could be attributed to schizophrenia. Nearly all victims of schizo-
admission between different European countries (Riecher-Rössler et al., 1991). In a representative survey in Switzerland, we could show that this is in line with the general public’s attitude: about 70% of the respondents agreed to compulsory admissions in case of serious mental illness (Lauber et al., 2000). Nevertheless, there are considerable differences in rates of compulsory admission between different European countries (Riecher-Rössler and Rössler, 1993; Salize and Dressing, 2004), which is by no means justified by objective reasons, but due more to differing legislation (Table 1).

Table 1
Rates of involuntary placements for mental disorder in European Union countries per 100,000 population

<table>
<thead>
<tr>
<th>Country</th>
<th>Rate (Year)</th>
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<tbody>
<tr>
<td>Austria</td>
<td>175 (1999)</td>
</tr>
<tr>
<td>Belgium</td>
<td>47 (1998)</td>
</tr>
<tr>
<td>Denmark</td>
<td>34 (2000)</td>
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<tr>
<td>Finland</td>
<td>218 (2000)</td>
</tr>
<tr>
<td>Germany</td>
<td>175 (2000)</td>
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<tr>
<td>Ireland</td>
<td>74 (1999)</td>
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<tr>
<td>Luxembourg</td>
<td>93 (2000)</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>44 (1999)</td>
</tr>
<tr>
<td>Portugal</td>
<td>6 (2000)</td>
</tr>
<tr>
<td>Sweden</td>
<td>114 (1998)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>48 (1999)</td>
</tr>
</tbody>
</table>

Data source: Salize and Dressing (2004).

8. Stigma

Negative attitudes towards the mentally ill, especially towards persons with schizophrenia, are widespread (Stuart and Arboleda-Florez, 2001). Individuals with schizophrenia are looked at frequently as being dangerous and unpredictable (Angermeyer and Matschinger, 2003). Many media reports reflect this fear; even if, in reality, a potential risk is mainly directed to the closest relatives (see above). This, and other stigmata attached to schizophrenia, creates a vicious cycle of discrimination leading to social isolation, unemployment, drug abuse, long-lasting institutionalisation or even homelessness—all factors that further decrease the chances of recovery and reintegration into normal life, in addition to the often-deleterious consequences of the illness itself.

On the basis of comprehensive research in this area during the last decade, several strategies were developed to fight stigma and discrimination because of schizophrenia. Within the framework of the global anti-stigma program “Open the Doors” of the World Psychiatric Association, different research centres developed interventions directed to specific target groups relevant for de-stigmatisation—e.g. students (Meise et al., 2000) or police officers (Pinfold et al., 2003). Interestingly, contact with the mentally ill seems to reduce social distance (Lauber et al., 2004) and predict a more positive attitude, which is a strong argument in favour of community psychiatry.

9. Cost

Although the financial aspects of schizophrenia only became an issue of psychiatric research within the general discussion concerning cost containment in health care, there is meanwhile enough evidence that schizophrenia has serious financial consequences for the patients, their relatives and the national economy (Rössler et al., 1998). Psychotic disorders are considered to be the most expensive mental illnesses in terms of costs of care per patient, accounting for 1.5% (UK), 2% (the Netherlands, France) or 2.5% (USA) of national health expenditures during the 1980s or 1990s (Knapp, 1997; Evers and Ament, 1995; Rouillon et al., 1994; Rupp and Keith, 1993). A most recent calculation estimated 1.3% health expenditures for schizophrenic patients in Germany in 2002 (Statistisches Bundesamt, 2004). Among all psychiatric disorders, only treatment and care for patients suffering from alcoholism or dementia might claim a greater proportion of the health care budgets of industrialised societies, but only due to a higher prevalence of these illnesses.

However, most cost-figures represent only expenditures for treated schizophrenic patients within the national health care systems. Although there are considerable efforts by the WHO and others to estimate the coverage and efficacy of mental health care worldwide, the proportions of schizophrenic patients who are treated in the national primary care or mental health care sectors, and how many remain untreated, is widely unknown. Only few studies assessed service use by schizophrenic patients. Estimates from the Epidemiological Catchment Area Program in the US show a 1-year service-use rate of about 60% of individuals with schizophrenia (Regier et al., 1993). Most probably, these proportions may vary with the specific conditions of the national health care systems.

The economic impact of schizophrenia is caused by the specific symptoms and characteristics of the disease as described above (e.g. early onset, frequently chronic course, early retirement, excess mortality, frequent readmissions to hospital treatment, high rate of disability, comprehensive rehabilitative needs). Although these characteristics imply enormous productivity losses, family financial burden and overall societal costs, little empirical data is available on secondary expenditures for schizophrenia. Its share of indirect costs is considered considerably higher than that for all other mental illnesses, which is estimated to be between 40% and 50% of the total financial burden for the economy.

Due to methodological problems, cross-national or pan-European studies aiming at standardised cost estimates are scarce, with only one study published during recent years (Knapp et al., 2002). Results from this study revealed...
considerable differences in the annual cost of care per patient (Fig. 2) between and within different countries (ranging from 2215 euros in Santander, Spain to 14,127 euros in Copenhagen, Denmark (unadjusted means, in 1998 prices)). Several national studies report a comparable (Salize and Rössler, 1996), even higher average annual cost of care (e.g. 18,038 euros for Germany, Salize and Stamm, 2004). These large differences are caused by several factors, mainly varying mental health care systems and quality standards of care (Salize et al., 1999).

Along with problems in evaluating the direct or indirect costs of schizophrenia, the cost-effectiveness analysis of essential aspects of care for schizophrenia patients is even more underdeveloped. There is a wide field of special treatments or care strategies in schizophrenia that whose cost impacts are worth analysis, i.e. quality of life in different treatments settings (Rössler et al., 1999). Nonetheless, cost-effectiveness research in schizophrenia has focused almost exclusively on pharmacological treatments, largely triggered by an ongoing international debate on the efficacy of so-called atypical neuroleptics, which are much more expensive than conventional drugs (Knapp, 2000).

10. Treatment

The treatment of schizophrenia rests on three main pillars. Firstly, there are medications to relieve symptoms and prevent relapse. Secondly, psychosocial interventions help patients and families to cope with the illness, and aim at preventing relapses. Thirdly, rehabilitation helps to reintegrate patients into the community and helps them to regain occupational functioning. The challenge in the care of people suffering from schizophrenia is the need to coordinate services, from early identification to regular treatment and rehabilitation. Currently, few patients with schizophrenia need long-term hospitalisation.

Antipsychotic medication has proved useful in reducing, and often eliminating, acute symptoms of schizophrenia, such as hallucinations and delusions. Medication status is the strongest predictor for relapse. Discontinuation of medication seems to increase the relapse risk about fivefold (Robinson et al., 1999).

Psychosocial intervention and rehabilitation for people with schizophrenia encompass a variety of measures from skills training or family interventions, to supported employment. The interactions between medication and psychosocial treatments appear to be more than merely additive, since each can enhance the effects of the other. Recent studies using newer antipsychotics suggest that these agents improve the participation of patients in psychosocial treatments (Marder, 2000). Four cognitive-behavioural approaches have emerged as being especially effective as adjuncts to pharmacotherapy, i.e. the training of social skills, cognitive training programs for the remediation of neurocognitive deficits, psychoeducative, coping-oriented interventions with patients and their families, and cognitive-behavioural therapy of residual symptoms (Brenner and Pfammatter, 2000).

With respect to the delivery of treatment and care, the process of deinstitutionalisation has led to fragmentation of services in the community. Lack of coordination and cooperation between services is the result and is one of the main reasons for the revolving-door phenomenon. Better coordination and cooperation are the major objectives of case management. However, research on case management is not conclusive. This might be due among others to the evident significant influence of national culture, both in the acceptability of case management and in approaches to researching it (Burns et al., 2001).

11. Early detection

Early detection and therapy of schizophrenic psychoses has become widely accepted goal in psychiatry. For example, the UK Government has decided to invest systematically in early detection and intervention, as “the rationale for early intervention is overwhelming” (Pelosi and Birchwood, 2003).

Whereas until some time ago early diagnosis and intervention in schizophrenia concentrated on clear-cut, frank schizophrenia, during recent years some centres have also started to treat patients, even before a clear diagnosis has been established. However, reliable methods for an early detection already in this phase of beginning schizophrenia do not yet exist, and the evidence base for treatment on the basis of psychosis-like experiences in the general population is thin (Hanssen et al., 2003).

Thus, one of the key questions for now is whether, and at what stage, early intervention, such as treatment with low-dose atypical neuroleptics, is indicated. This question confronts researchers and clinicians with the ethical
The rationale for early detection of schizophrenia is based on several observations:

- Diagnosis and treatment of schizophrenia are often seriously delayed. Thus, patients on average suffer from productive psychotic symptoms such as delusions or hallucinations for an average of 1–3 years before this disorder is diagnosed and treated for the first time (duration of untreated psychosis, DUP). In addition, even before then, patients suffer from an “unspecified prodromal phase” for an average of 2–5 years (duration of untreated illness, DII) (for reviews, see e.g. Norman and Malla, 2001; Bottlender and Möller, 2003; Riecher-Rössler et al., in press).

- Consequences of the disease are very severe already in the early preclinical, undiagnosed phase of the disorder. Even before first admission, most patients already suffer from serious impairments and losses in various social domains, such as education, work, partnership or independent living (Häfner et al., 1995). Recent studies have also shown that the quality of life is seriously impaired already at first admission and is associated with DUP (Brown et al., 2000).

- Early treatment seems to improve the course of the disease. There is a large body of evidence that the early treatment of psychosis can substantially improve the course and outcome of the disease (for reviews, see e.g. Norman and Malla, 2001; McGorry, 2002; Harrigan et al., 2003; Riecher-Rössler et al., in press). Thus, the majority of studies found a statistically significant correlation between a long duration of untreated psychosis (DUP) and a poor outcome.

The mechanisms by which DUP influences outcome could be manifold. Thus, ongoing psychosis could have direct “neurotoxic” effects, including neurodegeneration with symptomatic progression (Lieberman et al., 2001, Stahl, 2002) and cognitive deterioration (Amminger et al., 2003), although there are also studies that do not support this theory (e.g. Ho et al., 2003a,b). In any case, it is quite clear that the early treatment of frank psychosis can substantially ameliorate symptoms and shorten psychotic episodes (for review, e.g. Norman and Malla, 2001), and thereby avoid, or at least ameliorate, the immediate negative psychological and social consequences. Therefore, it can be stated quite safely that patients should be treated as early as possible as soon as frank psychosis has occurred. However, detection and treatment of the disorder even before that raises a number of questions that have not been sufficiently addressed as yet.

12. Gender issues

Gender differences in schizophrenia are well known. In particular, differences in age at onset have been confirmed in many studies. Less consistent are the findings concerning differences in symptomatology and the course of the disease, which might be due partly to methodological problems in earlier studies (for review, see Riecher-Rössler and Häfner, 2000; Riecher-Rössler and Rössler, 1998).

Methodologically sound studies (e.g. Sartorius et al., 1986; Jablensky et al., 1992; Hafner et al., 1989, 1993a,b) consistently showed a higher age of onset in women than in men. The average difference of 3.5–6 years was already evident at the first onset of early symptoms of the disease and was found in almost all cultures investigated.

The cumulative lifetime risk for men and women seems to be identical (Häfner et al., 1991a,b), although this has been questioned by a recent meta-analysis that, however, was based mainly on studies excluding older age groups (Aleman et al., 2003). In fact, men seem to show their peak of onsets in their early twenties and women theirs only in their late twenties; and there is a second, smaller peak of onsets in women after age 45 (Häfner et al., 1989, 1993a). Gender thus has no stable influence on the outbreak of the disease, but this influence is modulated by age—a finding that could be explained by a presumably protective effect of estrogens (Riecher-Rössler and Häfner, 1993; Riecher-Rössler, 2003).

As to symptomatology, it has often been reported that negative symptoms occur more frequently in men and affective symptoms more often in women. More recent studies have not consistently confirmed these findings (for review, see Riecher-Rössler and Häfner, 2000). Thus, gender differences in negative and affective symptoms seem to disappear if the sample is restricted to narrowly defined schizophrenia or to higher age groups. The few differences still found obviously have more to do with illness behaviour than with core symptomatology.

Women seem to have a more favourable course and a better psychosocial “outcome” than men (for review, see Riecher-Rössler and Rössler, 1998; Riecher-Rössler and Häfner, 2000). Their hospital stays were fewer and shorter, and their social adjustment and living situation better than those of men, whereas the symptom-related course seems to be similar for both genders. Women’s mortality is also lower, due mainly to their significantly lower suicide rate. Here again, more recent and reliable studies show that course does not differ between genders anymore if analyses...
are restricted to narrowly defined schizophrenia with a nuclear schizophrenic syndrome at onset. Furthermore, the better course of the disease was observed mainly in women up to menopause. The tendency for the better course in women could have to do with their later age of onset, which is associated with a better social integration, and with the protective effect of estrogens in young women (Navarro et al., 1996; Riecher-Rössler and Rössler, 1998).

The burden of the disease can be very different for men and women. Thus, e.g. the later age of onset in women means that they frequently have to cope with losses, e.g. in relationships or in the professional sphere. Men, due to their younger age, typically have not established themselves in these respects to the same extent at the onset of the condition. This means that for women the focus in therapy has to be the maintenance or reestablishment of certain roles, whereas for men the goal is often to attain certain roles for the very first time. In addition, gender-specific social roles, social status, social stress or social support can influence the course of the disease. For example, significantly more women than men with schizophrenia care for children (Seeman, 2004). The care for these children can be an enormous burden, with which these women so far get far too little help. In most European countries, there is a severe lack of assessment and treatment facilities for these mothers with their children, although the need for such facilities is well documented (Seeman, 2004; Mowbray et al., 2001; Oyserman et al., 1994).

There are times of an enhanced risk for an exacerbation of psychosis in women, dramatically so after parturition (Kendell et al., 1987), but also in perimenopause (see above) or perimenstrually (for review, see Riecher-Rössler, 2003). This puts a specific burden on women and needs a gender-sensitive therapeutic approach.

Consideration also needs to be given to the large field of gender-specific pharmacotherapy, e.g. the sex-specific treatment and side effects of neuroleptics (Goldstein et al., 2002). Hyperprolactinaemia-inducing neuroleptics, for example, can have severe short- and long-term consequences in women, such as premature menopause, osteopenia, etc. (Riecher-Rössler, 2003). It is not clear yet to which extent men are also affected by hyperprolactinaemia-induced side effects.

Men, on the other hand, not only need higher doses of neuroleptics (Goldstein et al., 2002), they also have specific needs in terms of psychosocial care. We have to be aware of their higher comorbidity—especially with respect to drugs and alcohol, and their higher risk of self-neglecting behaviour or suicide (Häfner et al., 1993a; Riecher-Rössler and Rössler, 1998).

13. Discussion

Although schizophrenia does not show a high incidence, due to the early age of onset and the often-chronic recurrent course, it shows a relatively high prevalence. This, and the fact that it often leads to mental and social disability, makes it one of the most burdensome and costly illnesses worldwide.

In addition to the direct burden, the affected persons are confronted with prejudice and discrimination. The stigma attached to schizophrenia creates a vicious cycle of discrimination leading to social isolation, unemployment, drug abuse, long-lasting institutionalisation or even homelessness, which further decreases the chances for recovery and reintegration into normal life.

The burden of schizophrenia can be very different in men and women, and the consequences of these differences for treatment and the provision of care have only begun to impact on professionals. Over the last decades, there has been considerable progress in treatment and care, with most efforts directed towards severely ill and chronic patients. Only recently has interest also been directed to early intervention, which might offer an opportunity to make a further major step towards positive changes in psychiatric practice. Yet it has to be stated that there are still many open research questions in this area.

A decrease in costs could be achieved mainly by a reduction in incidence; moderately, given an improvement in prognosis, and relatively minor, given the economies in direct treatment costs likely to follow a transfer to community treatment (Andrews, 1991). Current interventions avert some 13% of the burden, whereas 22% could be averted by optimal treatment (Andrews et al., 2003). Improvement in community treatment might also be associated with a further improvement of prognosis.

References


