

FREQUENCY AND LENGTH OF SCHIZOPHRENIA ADMISSIONS: ANALYSIS BY ICD-10 DEFINED SUBTYPES

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UDK: 616.895.5(497.5) Izvorni znanstveni rad Primljeno: 26. 9. 2000.

The frequency and length of admissions over 50 years were analyzed in a sample of 10.268 schizophrenic patients according to ICD-10 subtypes of schizophrenia. The lowest yearly hospitalization frequencies during the risk period were observed in simple, catatonic, unspecified and hebephrenic schizophrenia. When the total sample was analyzed, unspecified schizophrenia exhibited a significantly higher length of hospitalization than paranoid and undifferentiated/other schizophrenia. However, after the exclusion of continuous hospitalizations, unspecified schizophrenia, in severe contrast, was identified as the subtype with lowest admission length. This indicates the need for further research in order to explore the homogeneity of that diagnostic category, i.e. whether unspecified schizophrenia encompasses two subgroups with significantly different courses. Despite the fact that paranoid schizophrenia is generally considered as having the best course and prognosis, this subtype did not have the lowest frequency, nor length of hospitalization. A weak, but significant, negative correlation was observed between admission rate and the length of hospitalization for the total sample, and particularly in the paranoid and residual schizophrenia subtypes. In conclusion, subtypes of schizophrenia differ both in hospitalization rate and length of admission. The introduction of additional factors such as age at onset, gender, subtype presented at initial course of disorder or subtype stability during further analyses could help to identify groups that are more homogenous in their course, prognosis, and, possibly, etiology.

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INTRODUCTION

The chronic nature of this disorder, that impacts considerably on several areas of patient functioning, its unknown etiology, and high costs of care, have led to epidemiological schizophrenia research being used both as a means for delineating specific syndromes that could help in tracing the real cause of the illness, and as a tool for the improvement of health and social services for persons affected.

The International Classification of Diseases (ICD), in its 10th revision, divides schizophrenia into nine groups: paranoid, hebephrenic, catatonic, undifferentiated, residual, simplex, o-ther and unspecified schizophrenia, and postschizophrenic depression. Since past revisions have defined diagnostic categories in the schizophrenia group differently, the WHO issued conversion tables defining how subtypes listed in previous revisions should be converted to the most recent one (WHO, 1997).

Schizophrenia, as a chronic recurrent disorder, usually manifests itself during early adulthood, through to the end of life. Women were found to have a later average onset of disorder (Burack and Zigler, 1989), peaking between the ages of 20 and 29 (Hafner et al., 1991a), but differences between sexes may vary by cultures (Hambrecht et al., 1992), and the cumulative lifetime risk seems to be the same for both sexes (Hafner et al., 1991b). One large research even claimed a more favorable outcome for the disorder in females (Harrison et al., 1996), but exact neuropsychological or physiological evidence to support the hypothesis that gender is associated with the unique pathogenesis of schizophrenia, or is a marker for a distinct type of it, is still missing (Goldberg et al., 1995). It is still controversial whether late-onset schizophrenia is a separate entity, although some results lead in this direction (Jeste et al., 1995; Castle et al., 1997). Although 'age at onset' is conventionally synonymous to 'age at first admission', differences between sexes are not so apparent at the age at real onset (Folnegović-Śmalc et al., 1990), and the duration of the pre-hospitalization phase is significantly prolonged in the presence of positive familial loading (Mimica et al., 2000). When considering age at first admission among the schizophrenia group, the hebephrenic/ disorganized subtype demonstrated the earliest, and paranoid the latest, onset (Beratis et al., 1994). In reference to particular subtype disorder course, it was found that patients with an initial paranoid or positive episodes had a significantly better long-term outcome than patients having initial disorganized/ hebephrenic or catatonic episodes (Deister and Marneros, 1994). Paranoid schizophrenia is generally considered as the one with an older age at onset and good outcome or recovery, while hebephrenic and undifferentiated schizophrenia have an earlier age at onset and poorer long-term prognosis (Fenton and McGlashan, 1991). It appears that enduring negative and deficit symptoms

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY... may be particularly associated with a poor outcome (Mueser et al., 1991). One research concluded that readmission risk after first discharge decreases with increasing age and is also influenced by clinical subtype and gender, while, at later discharges, the effect of these variables gradually disappears (Mortensen and Eaton, 1994).

The long-term stability of subtypes is not considered the rule but the exception (Deister and Marneros, 1993). Most frequently, change occurs within the first few years of the illness with no clear direction, although disorder phenomenologies seem moderately stable (McGlashan and Fenton, 1993) in the first 5 years, but a substantial portion of schizophrenics are still re-hospitalized during the same period (Daniels et al., 1998). Among all subtypes, paranoid schizophrenia has the highest stability, hebephrenic schizophrenia stability is intermediate, and such stability in undifferentiated schizophrenia is virtually absent (Kendler et al., 1985). Paranoid, undifferentiated and hebephrenic subtypes do not seem to differ by gender, while the frequency in males can be up to three times higher for the residual and catatonic subtypes (Beratis et al., 1997).

The schizophrenia incidence rates in Croatia have shown to be consistently stable (Folnegović et al., 1990) in the range of 2,1 to 2,2 per 10.000. Although it is generally accepted that the incidence of the disorder is stable over time, some studies report that its incidence, at least expressed in admission rates, gradually decreases (Takei et al., 1996), a finding which could falsely present itself as seasonal changes in schizophrenia incidence rates (Henigsberg et al., 2000).

Because of the costs associated with the disorder, schizophrenia poses a major challenge to policy makers in health and social care (Kavanagh et al., 1995). In addition, research on the course of the illness is beneficial not only as a resource for helping health service systems to target management strategies (Kent et al., 1995), but also as a rare clue for understanding the etiology of the disorder (Lieberman et al., 1996), as well as for verification of group homogeneity as defined in currently used diagnostic instruments.

Frequency and duration of hospitalizations were rarely analyzed in larger samples according to schizophrenia subtype. In addition to gaining better insight in epidemiology of the disorder, this research could provide a basis for better cost-utilization in the offering of other health and community services for schizophrenic patients. Analysis done concerning all the patients in the schizophrenia group discovered that neither frequency, nor the duration of hospitalization, seem to be dependent on age groups (generations) or time periods (Gmur, 1987). Admission rates in terms of risk do not decrease with the stage of mental care deinstitutionalization (Sytema and Burgess, 1999; Appleby et al., 1993), but the duration of admission

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY...

METHODS

does (Tuori et al., 1998). Even in a deinstitutionalized environment, the brief-stay approach was questioned because it was shown that the likelihood that a brief-stay patient is re-hospitalized within one month after discharge is greater than in patients treated for longer periods (Appleby et al., 1993). The relation between the level of urbanization (Peen and Dekker, 1997) to the number and duration of hospitalizations is inverse to that of deinstitutionalization: at higher levels of urbanization, hospitalizations will be more numerous, but the level does not influence the duration of admission. The progressive nature of the disorder is also confirmed by the consistent finding that a higher number of subsequent admissions is related to higher number of admissions in the past period (Daniels et al., 1998; Munk-Jorgensen et al., 1991; Hoffmann, 1994).

The aim of this research was to identify possible differences in frequencies and duration of hospitalizations between various schizophrenia subtypes, as defined in the current ICD revision.

The frequencies and duration of admissions were analyzed on a sample group selected from the National Case Register maintained by the Croatian Institute of Public Health. Several criteria for inclusion into the sample to be analyzed were applied: (a) the patient must have a dissmission diagnosis (diagnosis at discharge from hospital) considered as schizophrenia in the current ICD revision; (b) schizophrenic patients must be permanent residents of Croatia; (c) the exact date-of-birth, and dates of admission and discharge for each hospitalization should be complete in the register entries; (d) the patient was born not earlier than 1944 and (e) the patient's first admission must be over one year before the end of the study period.

The frequencies and duration of hospitalizations during the period of 1950 to 1995 were analyzed in this research.

After several introductory years for reporting procedure and register maintenance, the National Case Register became fully operational in 1950. Reporting of every admission in a psychiatric hospital or in a general hospital psychiatric ward is obligatory and defined in health legislation. In addition to general data, this obligatory reporting includes the admission and release dates for every hospitalization. A group of experts periodically revise medical documentation for those patients who were dismissed during the past year with a diagnosis different from the previous one, and the current diagnosis is attributed to each patient. Following this procedure, after the ICD-10 became an official classification, each patient received an ICD-10 current diagnosis code, either by using the conversion procedures as defined by the WHO, or during their discharge from hospital.

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY...

From the total of 33.742 schizophrenic patient records in the register, only those patients whose diagnosis is consistent with ICD-10 criteria for schizophrenia were selected for analysis. Several diagnoses are no longer included in the schizophrenia group: in ICD-10 classification, latent schizophrenia (ICD 8,9 code 295.5) is now considered a schizotypal disorder (ICD-10 code F21); acute schizophrenic episode (295.4) is now grouped in acute and transient psychotic disorders (codes F23.1 or F23.2) and schizophrenic psychosis – schizoaffective type (295.7) now is in the schizoaffective disorders group (F25). In ICD-10, schizophrenic psychoses (295.8) is labeled as undifferentiated schizophrenia (F20.3), and post-schizophrenic depression (F20.4) is included in a group, having no equivalent code in past revisions. Those criteria limited the number to 30.831 patients in ICD-10 schizophrenia diagnostic categories. As conversion tables do not provide unidirectional instructions for conversion to undifferentiated and other schizophrenia, and since a number of patients have not been readmitted after ICD-10 became the valid classification, the group of undifferentiated and other schizophrenia were analyzed together in this study. The criterion concerning Croatian residency decreased the sample size by 6.331 patients who were residents of other countries and just treated in Croatian hospitals.

Out of the 24.500 patients who conformed to previous criteria, 10.864 were born after 1944. This year was chosen as a limit because the register became fully operational in 1950, although it was functional several years earlier, but the intention was to diminish the possibility that a patient was omitted because of undeveloped reporting procedures.

The upper boundary for the period being followed-up in this study was arbitrarily set to the beginning of 1995, but several reasons led to such a decision. First, in the years preceding that one, entries into the register were fully rechecked for incompleteness and clarified with the originating medical institutions. Second, we were able to trace the oldest patients in this research for 50 years, and there is no consensus in scientific sources whether schizophrenia onset at even older ages could be even considered as part of the same group or not. The other possibility would be to set the period that the patients were followed-up to some time-window, but this will additionally limit the sample without achieving a clear benefit.

Additional 596 patients were excluded due to missing data of birth or hospital admission/ discharge. That led to a number of 10.268 patients whose frequency and duration of hospitalizations were analyzed in this study.

Hospitalization frequencies were analyzed by the period in which there was a risk of readmission, the period being defined as beginning with the first hospitalization and ending with the close of the time interval that the patients were followed-

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY... -up (beginning of 1995). Therefore, hospitalization frequencies were calculated by dividing the total number of admissions with the duration of the risk period expressed in years.

Inter-group frequency differences in hospitalizations and duration of admissions were analyzed by ANOVA with the Scheffé-test for *post-hoc* analysis. Relationships between two variables were analyzed by linear correlation. In design of this study it was set that all statistical analyses will be performed at 5% level of significance.

Description of sample

In total 10.268 schizophrenic patients were included in the analysis, of them 6.183 (60,22%) were male and 4.085 (39,78%) female. By schizophrenia subtypes, the most numerous group in the analysis were schizophrenics suffering from paranoid schizophrenia – 4.128 of them, or 40,2% of the total sample, followed by the unspecified schizophrenia group with 3.477 patients (33,86%). Similar representation in the total sample was had by the 923 patients having undifferentiated and other schizophrenia (8,99%) and the 890 suffering from residual schizophrenia (8,67%). Simple schizophrenia had 493 patients (4,8%), while the lowest representation was amongst the hebephrenic (185 patients, or 1,8%) and catatonic schizophrenia (172, or 1,68%) subtypes.

At the time of analysis, the average age of the patients in the study was $38,48 \pm 7,22$ years. The respective ages of the following groups was near the mean for all schizophrenics: paranoid ($38,48 \pm 7,08$), unspecified ($38,52 \pm 7,24$), simple ($37,83 \pm 7,7$), undifferentiated/ other schizophrenia ($37,60 \pm 7,28$) and of catatonic ($39,03 \pm 7,75$), while the hebephrenic ($33,35 \pm 8,37$) and residual schizophrenia ($40,47 \pm 6,30$) groups were those with lowest and highest mean ages, respectively.

The mean hospitalization risk period, which was calculated as the time span between the age at first admission and the date a patient was followed-up, was $12,59 \pm 7,30$ years, and was comparable in all groups included: for paranoid schizophrenia it was $11,08 \pm 6,62$ years, in unspecified schizophrenia $13,38 \pm 7,44$ years, in undifferentiated/ other schizophrenia $12,68 \pm 7,36$ years, in residual schizophrenia $14,94 \pm 7,20$ years, in simple schizophrenia $14,14 \pm 8,15$ years, in hebephrenic schizophrenia $13,03 \pm 8,35$ years, and in catatonic schizophrenia the average period to patient followed-up was $15,52 \pm 8,63$ years.

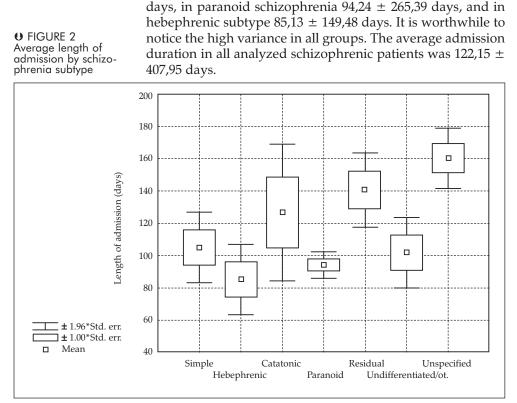
RESULTS

The average yearly number of hospitalizations during the risk period, displayed in Figure 1, shows that simple (0,426 \pm 0,460), catatonic (0,430 \pm 0,516) and unspecified schizophrenia (0,432 \pm 0,554) had a similarly low mean number of hospitalizations

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY...

• FIGURE 1 Mean number of yearly hospitalizations during the risk period, by schizophrenia subtype during the year, followed by the group with hebephrenic schizophrenia ($0,565 \pm 0,590$). On average, hospitalizations were more frequent in paranoid $(0,741 \pm 0,692)$, undifferentiated and other $(0,782 \pm 0,685)$ schizophrenia, while in the residual subtype $(0,895 \pm 0,682)$ hospitalizations were more than twice as frequent than in the three subtypes with the lowest hospitalization frequencies. This yielded high overall significant differences (ANOVA: SS_{effect}=298,65; df_{effect}=6; MS_{effect}=49,77; SS_{error}=4103,22; df_{error}=10261; MS_{error}=0,40; F=124,47; p<0,00001). Post-hoc analysis with the Scheffé test displayed 12 significant individual differences between every group with higher numbers of hospitalizations (paranoid, undifferented/other and residual schizophrenia) and each single group with a lower number of hospitalizations (simple, catatonic, unspecified and hebephrenic schizophrenia) – all of them far below a 1% level of significance, with the exception of those between paranoid and hebephrenic schizophrenia (p=0,03). In addition, significant differences were also observed between residual and paranoid (p < 0.0001) and residual and undifferentiated/other (p = 0.025)schizophrenia groups.

The highest average duration of admissions appeared among patients with unspecified schizophrenia (160,29 \pm 570,83 days), as displayed in the box and whisker plot in Figure 2. A somewhat lower duration of average admission was shown in residual (140,47 \pm 372,70) and in catatonic (126,48 \pm 287,88) subtypes. A rather lower and mutually similar duration of admissions was observed in the four remaining groups studied: in simple schizophrenia it was 104,67 \pm 247,54 days, in undifferentiated/other schizophrenia group it was 101,61 \pm 335,93



Although the admission duration differences showed high statistical significance between the seven analyzed groups (ANOVA: $SS_{effect}=9369842$; $df_{effect}=6$; $MS_{effect}=1561640$; $SS_{error}=1,7E+09$; $df_{error}=10261$; $MS_{error}=165603,9$; F=9,430; p<0,00001), the *post-hoc* analysis revealed only two significant differences, both involving the unspecified schizophrenia group: the first with the paranoid schizophrenia (p<0,001) group and the second with the group of undifferentiated/other schizophrenia (p=0,02).

Analysis of correlation between the number and length of admissions provided negative values when all schizophrenics were analyzed together (r=-0,10; p<0,001), and in each particular subtype group in the study, showing significance in the paranoid (r=-0,09; p<0,001), residual (r=-0,18; p<0,001), undifferentiated/other (r=-0,1; p=0,002) and unspecified schizophrenia groups (r=-0,09; p<0,001), but not in the simple (r=-0,08; p=0,06), hebephrenic (r=-0,04; p=0,62) and catatonic schizophrenia groups (r=-0,09; p=0,26).

The relation between the average number of hospitalizations per year and the mean length of stay in hospital is shown in Figure 3, displaying a progressive decrease in average admission length with an increase in the average number of ho-

120

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY...

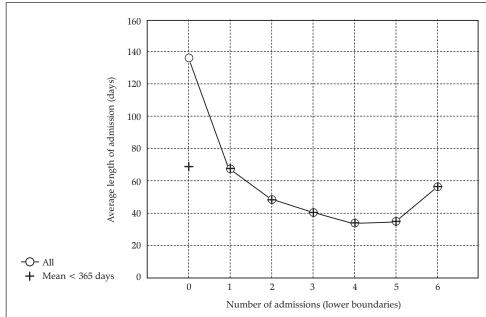
1,500 patients had more than 1, but less than 2 average hospitalizations per year, with an average hospitalization duration of 66,46 \pm 53,7 days; 304 patients had an average number of hospitalizations ranging between 3 and 3,99, and the average duration of admission was 40,26 \pm 23,68 days; 82 patients had between 4 and 4,99 admissions per year, with an average duration of 33,33 \pm 24,90 days; 9 patients had between 5 and 5,99 hospitalizations with an average duration of 35,72 \pm 8,38 days and 2 patients had between 6 and 6,99 average hospitalizations per year, with the average duration of 57,36 \pm 30,92 days. Two ranges were represented by only one patient and are not shown on this graph: the first fell in range of over 7 hospitalizations, having an average duration of 28 days, and the second patient had over 12 hospitalizations per year with the average length of stay of 15,76 days.

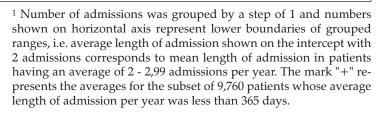
spitalizations per year. It shows that the decrease appears up

to the average of 4 hospitalizations, while from this value on-

ward the average length of hospitalization rises. A total of 8,345 patients had, on average, less than one hospitalization per year,

with an average hospitalization duration of $136,06 \pm 450,74$ days;





• FIGURE 3 Average length of admission by average number of admission per year¹

121

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY... A number of patients had year-long hospitalizations over a prolonged time. As these values could severely distort the overall averages, Figure 3 separately shows mean lengths of admission in 9,760 patients whose average hospitalization length was below 365 days, i.e. their hospitalizations were not continuous during the period analyzed. It should be noted that patients who were excluded fell into the first two numerical admission categories. In the sample subdivision, 7,842 patients who had an average number of hospitalizations less then 1 per year had a mean length of stay of 65,08 \pm 56,80 days, while the 1,495 patients with 1 – 1,99 average hospitalizations per year had an average length of admission which was 65,30 \pm 49,93 days. In this subdivision other values fully resemble those listed above for the entire analyzed sample.

For the subdivision of 9,760 patients whose average hospitalization length was less than 365 days, the average number of admissions and their duration, as well as the correlation between these two variables were calculated. As could be observed from Table 1, the average number of admission did not change considerably among individual subtypes. The mean length of admission for the unspecified schizophrenia subtype, having the highest average among all subtypes in the entire sample, ranks as the one with lowest average length of hospitalization, followed by similar averages in paranoid, undifferentiated/other and simple schizophrenia subtypes. The highest average duration of admission, when patients with yearlong stays were excluded, was observed in the catatonic, residual and hebephrenic schizophrenia subtypes.

• TABLE 1 Average number of admissions during risk period, their average length and correlation between these two variables, for the subset of patients not continuously hospitalized

		Number of admissions		Length of admissions			
Subtype	Ν	Mean		Mean	Std. Dev.	r	p (r)
Paranoid	3.989	0,75	0,70	63,75	52,59	-0,06	0,0005
Unspecified	3.235	0,45	0,57	61,12	55,54	-0,03	0,1303
Undifferentiated/ other	890	0,80	0,69	64,89	51,93	-0,05	0,1343
Residual	826	0,94	0,69	74,40	61,12	-0,12	0,0007
Simple	472	0,43	0,47	63,93	59,05	-0,03	0,4874
Hebephrenic	183	0,57	0,59	71,59	60,63	0,07	0,3754
Catatonic	165	0,44	0,52	77,11	57,43	-0,05	0,5283
Schizophrenia total	9.760	0,65	0,67	64,26	54,97	-0,04	0,0003

When continuous hospitalizations were excluded, the same significant differences in the number of admissions remains as when the total sample was analyzed. Analysis of admission duration (ANOVA) between all groups still shows high statistical significance (p<0,0001). However, some individual intergroup differences became reversed: unspecified schizophrenia, which became the subtype with lowest mean length of admissions, displayed significant differences with residual (p<0,0001)

and catatonic (p=0,038) schizophrenia. Two additional differences were also observed, both involving residual schizophrenia: the first was with the paranoia group (p=0,002) and the second was with the undifferentiated/other schizophrenia group (p=0,045).

DISCUSSION

In this research we limited our interest only to those diagnostic categories that according to recent ICD classifications are considered schizophrenia. The recent revision provided more clarity in definition of schizophrenia and has excluded disorders that are either transient in duration or that share more characteristics with other groups than with schizophrenia. By applying that criterion we believe that we have achieved better sample homogeneity.

As our sample did not include patients older than 50 years of age, the observed larger proportion of males supports previous findings concerning the later onset of the disorder in females (Burack and Zigler, 1989) and a higher proportion of late-onset schizophrenia in females (Lindamer et al., 1999). The finding that neither frequency, nor the duration, of hospitalization was found to be dependent on age groups or time period (Gmur, 1987) provides the basis for the assumption that the differences in mean ages between the analyzed groups did not influence the results.

It is a commonly held belief that paranoid schizophrenia is associated with a more moderate course and that the course of hebephrenic schizophrenia is associated with a poorer outcome, a notion supported by some studies (Deister and Marneros, 1994; Fenton and McGlashan, 1991). Results presented here do not provide a basis for reaffirming such beliefs. In our sample patients, hebephrenic schizophrenia showed a significantly lower number of admissions than paranoid schizophrenia and a lower, although not statistically significant, mean length of hospitalizations when the total sample was analyzed. Even when patients with continuous hospitalizations were excluded, which represented a higher proportion in the paranoid subtype, significant differences between these two subtypes were still not observed. Paranoid schizophrenia was neither among the subtypes with the lowest frequency of hospitalizations during the risk-period, nor was it the subtype with the lowest average duration of admissions in both analyses performed.

Results for the hebephrenic schizophrenia group are totally unexpected and even surprising. In addition to the already mentioned lower number of hospitalizations during the risk period observed in comparison with paranoid schizophrenia,

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY... this subtype also displayed significant differences compared to the group of undifferentiated and other schizophrenia and the group of residual schizophrenia. Also, the average duration of admission for this group did not produce any significant differences against all the other subtypes in the analysis, neither when the total sample was analyzed, nor when patients with continuous hospitalizations were excluded. Prior to exploring the possibility of reconsidering the postulate concerning a more severe course in hebephrenic schizophrenia, several warnings should be emphasized. First, patients with hebephrenic schizophrenia had a somewhat lower average age then the patients in the other groups. Although it could be that patients with hebephrenic schizophrenia were followed--up in this research for a comparable period as with the groups, the possibility still remains that frequency and duration of hospitalization after the follow-up period in this study could become more frequent and prolonged. Second, some patients, now entered into the residual subtype, initially originated from the hebephrenic one. The highest stability was found in the paranoid subtype and intermediate stability was found in the hebephrenic subtype (Kendler et al., 1985) indicating that the number of patients converted to residual schizophrenia was not excessively large. A portion of former hebephrenic patients now described as having residual schizophrenia certainly contributed to the lower mean age of patients observed in the hebephrenic schizophrenia group. Still, residual schizophrenia is listed as a separate diagnostic entity in the most recent ICD and DSM classifications, and we felt it more appropriate to analyze patients by their current diagnosis, rather than to analyze them by the diagnostic categories to which they belonged to in the past. Therefore, our results are not in direct contradiction with those showing that patients with paranoid episodes had a significantly better long-term outcome than those with hebephrenic episodes (Deister and Marneros, 1994), because the cited research studied patients according to their initial, rather then current, diagnosis. Third, sample size in hebephrenic schizophrenia was considerably smaller than in the other subtypes, with the exception of catatonic schizophrenia. However, the standard mean error, as a function of the variance and sample size, is comparable to the majority of other subtypes analyzed, at least when the total sample was analyzed. It is important to note that in the study we could not increase the sample size for the same period to obtain more precise confidence intervals to reveal possible differences not noticed here. This could be done only in the registers of countries with larger populations.

Unspecified schizophrenia could obviously be characterized as a subtype with low admission rates.

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY...

Two observations may indicate the possible existence of two subdivisions in the unspecified schizophrenia category. First is the finding that this subtype, as the one with the highest admission length when the full sample was studied, became the one with lowest length after the continuous hospitalizations were excluded. The second one is the related finding that this subtype has the second highest ratio of unbroken admissions. Both subdivisions of unspecified schizophrenia could be characterized by low admission rates, but the underlying reasons could be completely opposite. The first subdivision may be remittent in nature, requiring infrequent and brief hospitalizations followed by a relatively long remission period. The second assumed subdivision could also be described as having infrequent hospitalizations, but the low frequencies could be caused by the deteriorating nature of the disorder which rarely enables a patient to even leave the hospital. At this stage of research it is not possible to properly confirm this assumption, but it would be beneficial if additional studies were to explore whether unspecified schizophrenia could be better specified.

The different relationship between individual schizophrenia subtypes in number and duration of admissions, which was observed when patients with continuous hospitalizations were excluded, is obviously caused by the fact that such hospitalizations were not equally represented in each particular subtype. The overall reduction of sample size was 4,95%, in residual and unspecified schizophrenia this reduction was particularly high (7,19% and 6,96%, respectively), while in hebephrenic schizophrenia it was remarkably low (1,08%). This points to the necessity of further research in order to confirm and additionally explore the reasons underlying such differences in year(s)-long hospitalizations. While in residual schizophrenia this large proportion could be attributed to persistent sequelae of previously existing subtypes, it seems worthwhile to research whether the high proportion of prolonged episodes in unspecified schizophrenia, and low proportion of them in hebephrenic schizophrenia, are genuine characteristics of these subtypes.

It is interesting to note that analysis of length of admissions in residual schizophrenia, after continuous hospitalizations were excluded, did not produce such profound changes as were observed in unspecified schizophrenia, although residual schizophrenia was the subtype with the highest share of continuous hospitalizations (over 7%). Even before and after continuous admissions were excluded, this subtype remained the second highest in average duration of hospitalization. The finding that the residual subtype displayed the high-

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY... est admission rate, showing statistical significance in comparison with every other subtype, leads to a confirmation of its progressive nature, requiring long duration admissions, and where possible disruption of hospital treatment could be compensated by high admission rates.

The common problem of subtype instability over time (Deister and Marneros, 1993) plagues almost all epidemiological schizophrenia studies going beyond the initial period of stability at presentation of the disorder (McGlashan and Fenton, 1993), because of the difficult decision of whether patients should be followed-up according to their initial or current diagnosis. The existence of residual schizophrenia as a diagnostic category gives researchers particular doubts. This category confounds virtually all epidemiological studies involving schizophrenia subtypes. A residual schizophrenia might be viewed as closer to being a course identifier of the disorder than a separate diagnostic entity. Although not frequently mentioned explicitly, this uncertainty concerning the position of residual schizophrenia is reflected with the exclusion of residual schizophrenia from analysis of schizophrenia subtype characteristics in recent research. However, only extensive research concerning the onset and course of residual schizophrenia can determine whether there is a need to list residual schizophrenia as a separate diagnostic entity or not.

The finding that patients from the overall sample having less than one hospitalization per year during their risk-period have the highest average duration of admission (Figure 3) is not surprising, since year-long hospitalized patients shift the average of admission length considerably upwards. But it was not expected that, when patients having continuous hospitalizations were excluded, the patients having an average of less than one hospitalization per year had only a slightly lower average length of stay in hospital than those who had between one and two hospitalizations per year. The shape of the curve implies that patients who have higher average frequency of hospitalizations also have shorter admission duration than those who have lower frequencies. This finding could be explained by the increased probability that more frequently hospitalized patients receive appropriate medicines and drug regimens and that hospitalizations are needed only for smaller scale therapy corrections. The curve on the same graph also indicates that, after reaching a trough at about 4 hospitalizations per year, the average length of stay increases with higher hospitalization frequencies. This finding should be interpreted cautiously, as the number of patients having higher frequencies in admissions falls rapidly, and only 9 patients had between 5 and 6 hospitalizations, on average. However, interpretation of the results discussed here is further compli-

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY... cated by the fact that longer duration of admission reduces the chances for rehospitalization in the remainder of the year. Still, what could be hypothesized is that lower frequency in admission is not necessarily a predictor for shorter duration, or, put otherwise, that lower admission length is not necessarily associated with lower frequency of admission in the remaining period. This is compatible with a finding previously described (Appleby, 1993). The highly significant correlation observed in the paranoid and residual subtypes indicates that increased frequency of hospitalizations as a predictor of shorter admissions might be more regularly met in these two subtypes than in others.

Our research covered a 50-year period during which considerable social changes and overall societal development occurred. However, the possible increase in frequency of hospitalizations that correlates with the level of urbanization (Peen and Dekker, 1997) or the decrease in admission length that correlates with the stage of mental care deinstitutionalization (Sytema and Burgess, 1999; Appleby et al., 1993) may lead to changes reflecting the overall schizophrenic patient population. Since schizophrenics of all subtypes could have been irrespectively affected with these changes, the afore-mentioned correlations did not influence our subtype comparison results to any major extent, which was the aim of our research.

Every single analysis in our research displayed significant differences among schizophrenia subtypes. Subtypes of schizophrenia differ by hospitalization rate, length of admission, and correlations between these two variables. The analysis of hospitalization frequency and average duration is only one aspect of exploring differences in course and disorder prognosis. The introduction of additional factors into further analyses could help to identify groups that are even more homogenous in their course, prognosis, and, possibly, etiology. One of them could be the age at onset of disorder. Exploration should be done to find whether hospitalization frequencies and duration exhibit the same functional dependence on the time elapsed before the disorder becomes clinically apparent, equally in all subtypes. In addition, several other factors could also be helpful in discovering individual schizophrenia subtype course specificities, or even subgroups inside them. Examples could be the analysis of the ratio between relapses requiring hospital treatment and period of remissions, subtype presented at initial admission and subtype stability over time. Despite the fact that the diagnostic approach to schizophrenia was subject to considerable improvement in the past decade, the still unknown etiology of the disorder urges the need for even more distinctive delineation between different diagnostic categories now in the schizophrenia group.

REFERENCES

Appleby, L., Desai, P. N., Luchins, D. J., Gibbons, R. D., Hedeker, D. R. (1993). Length of stay and recidivism in schizophrenia: a study of public psychiatric hospital patients, *Am J Psychiatry*, 150(1), 72-76.

Beratis, S., Gabriel, J., Hoidas, S. (1994). Age at onset in subtypes of schizophrenic disorders, *Schizophr Bull*, 20(2), 287-296.

Beratis, S., Gabriel, J., Hoidas, S. (1997). Gender differences in the frequency of schizophrenic subtypes in unselected hospitalized patients, *Schizophr Res*, 23(3), 239-244.

Burack, J. A., Zigler, E. (1989). Age at first hospitalization and premorbid social competence in schizophrenia and affective disorder, *Am J Orthopsychiatry*, 59(2), 188-196.

Castle, D. J., Wessely, S., Howard, R., Murray, R. M. (1997). Schizophrenia with onset at the extremes of adult life, *Int J Geriatr Psychiatry*, 12(7), 712-717.

Daniels, B. A., Kirkby, K. C., Hay, D. A., Mowry, B. J., Jones, I. H. (1998). Predictability of rehospitalisation over 5 years for schizophrenia, bipolar disorder and depression, *Aust N Z J Psychiatry*, 32(2), 281-286.

Deister, A., Marneros, A. (1993). Long-term stability of subtypes in schizophrenic disorders: a comparison of four diagnostic systems, *Eur Arch Psychiatry Clin Neurosci*, 242(4), 184-90.

Deister, A., Marneros, A. (1994). Prognostic value of initial subtype in schizophrenic disorders, *Schizophr Res*, 12(2), 145-157.

Fenton, W. S., McGlashan, T. H. (1991). Natural history of schizophrenia subtypes. I. Longitudinal study of paranoid, hebephrenic, and undifferentiated schizophrenia, *Arch Gen Psychiatry*, 48(11), 969-977.

Folnegović, Z., Folnegović-Šmalc, V., Kulčar, Z. (1990). The incidence of schizophrenia in Croatia, *Br J Psychiatry*, 156, 363-365.

Folnegović-Šmalc, V., Folnegović, Z., Kulčar, Z. (1990). Age of disease onset in Croatia's hospitalized schizophrenics, *Br J Psychiatry*, 156, 368-372.

Gmur, M. (1987). Die Wandlung der hospitalisierungsdauer und hospitalisierungshaufigkeit von schizophrenen – Eine uberprufung an einer alteren und einer jungeren generation sozialpsychiatrisch behandelter patienten, *Soz Praventivmed*, 32(3), 137-139.

Goldberg, T. E., Gold, J. M., Torrey, E. F., Weinberger, D. R. (1995). Lack of sex differences in the neuropsychological performance of patients with schizophrenia, *Am J Psychiatry*, 152(6), 883-888.

Hafner, H., Behrens, S., De Vry, J., Gattaz, W. F. (1991a). Oestradiol enhances the vulnerability threshold for schizophrenia in women by an early effect on dopaminergic neurotransmission. Evidence from an epidemiological study and from animal experiments, *Eur Arch Psychiatry and Clin Neurosci*, 241(1), 65-68.

Hafner, H., Riecher, A., Maurer, K., Fatkenheuer, B., Loffler, W., an der Heiden, W., Munk-Jorgensen, P., Stromgren, E. (1991b). Sex differences in schizophrenic diseases, *Fortschr Neurol Psychiatr*, 59(9), 343-360.

Hambrecht, M., Maurer, K., Hafner, H. (1992). Gender differences in schizophrenia in three cultures. Results of the WHO collaborative study on psychiatric disability, *Soc Psychiatry Psychiatr Epidemiol*, 27(3), 117-121.

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY... Harrison, G., Croudace, T., Mason, P., Glazebrook, C., Medley, I. (1996). Predicting the long-term outcome of schizophrenia. *Psychol Med*, 6(4), 697-705.

Henigsberg, N., Folnegović-Šmalc, V., Moro, LJ. (2000). Seasonality of schizophrenic birth: possibly neither artifact, nor universal finding, *Nordic Journal of Psychiatry* (in press).

Hoffmann, H. (1994). Age and other factors relevant to the rehospitalization of schizophrenic outpatients, *Acta Psychiatr Scand*, 89(3), 205-10.

Jeste, D. V., Harris, M. J., Krull, A., Kuck, J., McAdams, L. A., Heaton, R. (1995). Clinical and neuropsychological characteristics of patients with late-onset schizophrenia, *Am J Psychiatry*, 152(5), 722-730.

Kavanagh, S., Opit, L., Knapp, M., Beecham, J. (1995). Schizophrenia: shifting the balance of care, *Soc Psychiatry Psychiatr Epidemiol*, 30(5), 206-212.

Kendler, K. S., Gruenberg, A. M., Tsuang, M. T. (1985). Subtype stability in schizophrenia, *Am J Psychiatry*, 142(7), 827-832.

Kent, S., Fogarty, M., Yellowlees, P. (1995). Heavy utilization of inpatient and outpatient services in a public mental health service, *Psychiatr Serv*, 46(12), 1254-1257.

Lieberman, J. A., Koreen, A. R., Chakos, M., Sheitman, B., Woerner, M., Alvir, J. M., Bilder, R. (1996). Factors influencing treatment response and outcome of first-episode schizophrenia: implications for understanding the pathophysiology of schizophrenia. *J Clin Psychiatry*, 57 Suppl. 9, 5-9.

Lindamer, L. A., Lohr, J. B., Harris, M. J., McAdams, L. A., Jeste, D. V. (1999). Gender-related clinical differences in older patients with schizophrenia, *J Clin Psychiatry*, 60(1), 61-67.

McGlashan, T. H., Fenton, W. S. (1993). Subtype progression and pathophysiologic deterioration in early schizophrenia, *Schizophr Bull*, 19(1), 71-84.

Mimica, N., Henigsberg, N., Folnegović-Šmalc, V., Uzun, S. (2000). The role of type, sex and familial loading in pre-hospitalisation interval (in submission).

Mortensen, P. B., Eaton, W. W. (1994). Predictors for readmission risk in schizophrenia, *Psychol Med*, 24(1), 223-232.

Mueser, K. T., Douglas, M. S., Bellack, A. S., Morrison, R. L. (1991). Assessment of enduring deficit and negative symptoms subtypes in schizophrenia, *Schizophr Bull*, 17(4), 565-82.

Munk-Jorgensen, P., Mortensen, P. B., Machon, R. A. (1991). Hospitalization patterns in schizophrenia. A 13-year follow-up, *Schizophr Res*, 4(1), 1-9.

Peen, J., Dekker, J. (1997). Admission rates for schizophrenia in The Netherlands: an urban/rural comparison, *Acta Psychiatr Scand*, 96(4), 301-305.

Sytema, S., Burgess, P. (1999). Continuity of care and readmission in two service systems: a comparative Victorian and Groningen case-register study, *Acta Psychiatr Scand*, 100(3), 212-9.

Takei, N., Lewis, G., Sham, P. C., Murray, R. M. (1996). Age-period-cohort analysis of the incidence of schizophrenia in Scotland, *Psychol Med*, 26(5), 963-973.

HENIGSBERG, N., FOLNEGOVIĆ-ŠMALC, V.: FREQUENCY... Tuori, T., Lehtinen, V., Hakkarainen, A., Jaaskelainen, J., Kokkola, A., Ojanen, M., Pylkkanen, K., Salokangas, R., Solantaus, J., Alanen, Y. (1998). The Finnish National Schizophrenia Project 1981-1987: 10-year evaluation of its results, *Acta Psychiatr Scand*, 97(1), 10-17.

World Health Organization (1997). Conversion table between ICD-10, ICD-9 and ICD-8 of Chapter V Mental and Behavioural Disorders, Copenhagen, World Health Organization.

Učestalost i trajanje hospitalizacija shizofrenih bolesnika: analiza prema MKB-10

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Učestalost i trajanje hospitalizacija kroz 50 godina analizirani su na uzorku od 10 268 shizofrenih bolesnika s obzirom na podtip shizofrenije prema MKB-10. Najmanja učestalost hospitalizacija po godini rizika opažena je kod jednostavne, katatone, nespecificirane i hebefrene shizofrenije. U ukupnom uzorku, kod nespecificirane se shizofrenije uočava značajno veće trajanje hospitalizacija nego kod paranoidne te nediferencirane i druge shizofrenije. Nakon isključenja iz analize onih ispitanika kod kojih postoji trajna hospitalizacija tijekom promatranih godina, nespecificirana shizofrenija se, potpuno obratno, izdvaja kao podtip s najmanjim trajanjem hospitalizacije, što upućuje na potrebu daljnjih istraživanja s ciljem ustanovaljavanja prave homogenosti te dijagnostičke kategorije, odnosno obuhvaća li taj podtip dvije skupine potpuno suprotnog tijeka bolesti. Usprkos tome što se paranoidna shizofrenija načelno smatra podtipom s najpovoljnijim tijekom i prognozom bolesti, u ovom se istraživanju on ne pokazuje niti kao onaj s najmanjom učestalosti hospitalizacija, a niti kao onaj s njihovim najmanjim trajanjem. Slaba, ali statistički značajna negativna korelacija uočava se između učestalosti hospitalizacija i njihova trajanja kada su svi shizofreni ispitanici analizirani zajedno, a kod pojedinih podtipova takva se korelacija opaža kod paranoidne i rezidualne shizofrenije. Zaključno, podtipovi shizofrenije razlikuju se i po učestalosti hospitalizacija i po njihovu prosječnom trajanju, a uključivanje dodatnih čimbenika u budućim analizama (kao što su dob nastupa poremećaja, spol, podtip koji se očitovao u početku bolesti, ili promjenjivost dijagnostičke kategorije) može pridonijeti prepoznavanju podskupina koje su u većoj mjeri homogene s obzirom na tijek i prognozu, a, moguće, i na svoju etiologiju.

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Häufigkeit und Dauer von Krankenhausaufenthalten schizophrener Patienten: eine Analyse gemäß ICD-10

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Zum Zweck der vorliegenden Untersuchung wurden 10.268 Fälle schizophrener Patienten analysiert, die im Laufe der letzten 50 Jahre wiederholt hospitalisiert worden waren. Die Häufigkeit und Dauer von Krankenhausaufenthalten wurde bei solchen Patienten ausgewertet, bei denen gemäß den unter ICD-10 aufgelisteten Kriterien ein spezifischer Untertypus von Schizophrenie vorliegt. Die geringste Zahl von Krankenhausaufenthalten je Risikojahr war bei Fällen von katatonischer, nichtspezifizierter und hebephrener Schizophrenie zu beobachten, wohingegen es bei undifferenzierter sowie einigen anderen Arten von Schizophrenie zu weitaus häufigeren Hospitalisierungen kam. Nachdem jene Patienten, die sich zu Dauerbehandlungen in Krankenhäusern befinden, aus der Analyse ausgesondert worden waren, stellte sich heraus, dass im Gegensatz dazu nichtspezifizierte Schizophrenie jene Erkrankungsform darstellt, die mit den kürzesten Hospitalisierungen verbunden ist. Dieser Umstand erfordert weitere Untersuchungen, um das wahre Homogenitätsniveau dieser diagnostischen Kategorie zu ermitteln und eine Antwort auf die Frage zu finden, ob dieser Untertypus von Schizophrenie zwei völlig voneinander abweichende Manifestationsformen umfasst. Obwohl wiederum paranoide Schizophrenie generell als die Erkrankungsform mit dem günstigsten Verlauf und den günstigsten Besserungsaussichten gilt, zeigte sie in dieser Untersuchung weder die geringsten Krankenhausaufenthalte, noch waren diese von der kürzesten Dauer. Ein schwacher, aber statistisch dennoch relevanter negativer Bezug war zwischen der Häufigkeit von Hospitalisierungen und ihrer Dauer zu beobachten, nachdem sämtliche schizophrene Patienten analysiert worden waren; dies galt insbesondere für die diagnostischen Kategorien der paranoiden und residualen Schizophrenie. Abschließend kann gesagt werden, dass sich die verschiedenen Erkrankungsformen sowohl in der Häufigkeit von Krankenhausaufenthalten als auch in deren Dauer unterscheiden. Zukünftige Analysen sollten zusätzliche Faktoren mit einschließen, so etwa das Alter, in dem eine Erkrankung zum ersten Mal auftrat; das Geschlecht des/der Erkrankten; die bei Krankheitsbeginn erstellte Diagnose; die Veränderlichkeit der diagnostischen Kategorie. Auf diese Weise können die einzelnen Manifestationsformen von Schizophrenie, die hinsichtlich Krankheitsverlauf und Aussichten, aber vermutlich auch hinsichtlich der Atiologie eine größere Homogenität aufweisen, besser erkannt werden.