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Gender differences in the prediction of 5-year outcome in first episode psychosis

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Abstract

Objective: *To examine gender differences in prediction of long-term outcome in first episode psychosis (FEP).*
Method: *Eighty-one male and 72 female FEP patients were compared regarding the sensitivity and specificity of the Predictive Rating Scale (PRS). The contributions of pre-admission clinical and socio-demographic characteristics to a poor 5-year outcome were analysed for males and females separately. Gender differences in the relations between predictors and outcome were examined using the equality of correlation comparing correlation coefficients.*
Results: *The sensitivity of the PRS was significantly better for males than for females. The following items: 'the highest Global Assessment of Functioning (GAF) the year before first admission ≤70' and 'GAF at first admission ≤30' explained most of the variance of a poor 5-year outcome for males, whereas for females the corresponding items were 'the highest educational level is compulsory school', 'living with parents' and 'contact with friends ≤2–3 times/month'. When the PRS was adapted assigning a weight of two to the item 'the highest educational level is compulsory school' for females, the sensitivity increased.*
Conclusion: *This study revealed that the predictors for poor outcome differ between male and female patients with FEP.*

Key words: gender differences, psychosis, outcome

Introduction

In the long term about half of the patients suffering from psychosis recovered or lived a 'full life'. The other half appeared to show a poorer outcome with disabilities and difficulties in everyday life that affected work/studies, social relations and independent living (Bleuler, 1974; Ciompi, 1980; Harding et al., 1987; Huber et al., 1980; Tsuang et al., 1979). To further optimize treatment it is crucial to identify patients at risk of an unfavourable long-term outcome in the early stages of psychosis. One way to identify those at risk is to use predictive scales, such as, those developed by Vaillant, Stephens, Philips and Strauss–Carpenter (Phillips, 1953; Stephens et al., 1997; Strauss and Carpenter, 1974; Vaillant, 1964). Among these the Strauss–Carpenter outcome scale had the best predictive power when re-tested in a new sample. However, the scale includes 'days spent in hospital' as a predictor and due to the changed focus from inpatient to outpatient care this is now inadequate.

Recently developed by the present authors, the Predictive Rating Scale (PRS), showed that five items obtained at first admission fairly accurately could predict unfavourable outcome among first episode psychosis (FEP) patients (Flyckt et al., 2006). These items are: 'the highest Global Assessment of Functioning

(GAF) the year before first admission ≤70', 'the highest educational level achieved: just compulsory school', 'the GAF at first admission ≤30', 'male gender' and 'contact with friends not more than 2–3 times per month'. These items showed a predictive potential of 81% (sensitivity 77%, specificity 84%). In the PRS each item renders a score of one point and none of the items are weighted. The scale has not yet been validated in an independent sample of FEP patients.

It is well known that male and female patients with psychosis differ with regard to many aspects. Males more often have an earlier onset, show a lower pre-morbid level of functioning, have more negative and less affective symptoms and more often face a poor outcome compared to females (Foerster et al., 1991; Hafner, 2003; Lindamer et al., 2003; Preston et al., 2002; Salokangas et al., 2003; Usall et al., 2003). Although differences in prognosis between males and females with psychoses are well known, few studies compare outcome between males and females with psychosis in the long term. Larsen et al. (2000) noted that gender differences influenced the relation between duration of untreated psychosis (DUP) and 1-year outcome. Among males there was a significant correlation between long DUP and a low score on the GAF and a high sum score of positive symptom score whereas among females long DUP was related to a high sum score of negative symptoms. Larsen et al. (2000) concluded that gender differences should be addressed in future research on psychosis. Among the predictive scales mentioned earlier, the PRS is the only one that includes gender as a predictor (Flyckt et al., 2006).

Apart from being correlated with gender, long-term outcome has also been reported to be correlated with several other characteristics such as age at onset, education level, pre-morbid functioning, DUP, symptoms and the type of diagnosis for patient with psychoses (Amminger et al., 2002; Carbone et al., 1999; Drake et al., 2000; Flyckt et al., 2006; Harrigan et al., 2003; Harris et al., 2005; Larsen et al., 2000; Malla et al., 2002; Marshall et al., 2005; Norman et al., 2005; Perkins et al., 2005). Because all of these variables are available at the first admission of a FEP patient, making a prognosis is possible. In addition, a positive clinical outcome in FEP is to be related to a lesser reduction in the level of general cognitive abilities assessed at the time of admission as compared with the estimated pre-morbid level and better performance on visual and verbal memory tests (Verdoux et al., 2002). Patients with a risk of continued psychotic illness are characterized by lower performance on non-verbal than on verbal tests (Amminger et al., 2000; Iverson et al., 2001) and deficits in memory, attention, psycho-motor speed and executive functions (Egeland et al., 2003). Deficits in cognitive functioning can predict a reduced level of social functioning and reduced work capacity (Green et al., 2000). A recent study from our group found that cognitive performance at admission predicted 3-year outcome in FEP patients (Carlsson et al., 2006).

The study examines whether PRS had an equally predictive potential for both males and females and whether the constellation of predictors differed between the genders. In addition this study examines gender differences in pre-admission and baseline clinical and socio-demographic characteristics and their impact on 5-year outcome.

Methods

The study sample is derived from the Parachute Project, a study representing an effort to provide immediate need-adapted treatment for FEP patients (Alanen et al., 1991). However, no special strategies were used to decrease DUP, which separates the Project from most 'early intervention' projects. The recruitment area covered both rural and urban areas including one-sixth of the Swedish population. The study included FEP patients from 17 psychiatric clinics with an onset of FEP from January 1996 to December 1997. To be included in the study the patient had to be between 18–45 years old and the exclusion criteria were a serious somatic illness, dominating substance abuse or neurological disorders. One hundred and seventy-five patients gave informed consent and were included in the study and 153 remained at the 5-year follow-up; a non-participant analysis is reported in a previous study (Cullberg et al., 2002). All patients underwent extensive somatic, neurological and psychiatric examinations including a checklist of background variables (Table 1) and a series of rating scales covering symptoms, Brief Psychiatric Rating Scale (BPRS) and social functioning, Strauss–Carpenter outcome scale, GAF. The diagnosis was set with a structured diagnostic interview, Structured Clinical Interview for DSM-IV (SCID) (Spitzer, 1987). Based on the diagnostic classification all patients were divided into schizophrenia syndrome diagnosis (schizophrenia, schizophreniform and schizo-affective psychoses) and non-schizophrenia syndrome (brief psychotic episode, delusional disorders, affective

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Table 1. Baseline characteristics in male ($n = 81$) and female ($n = 72$) patients with first episode psychosis. The total number of patients with data is reported in each item (n)

Characteristics	Males	Females
Age, mean, median, standard deviation (n)	27.9, 26.7, 6.2 (81)	29.6, 29.1, 7 (72)
DUP, mean, median, standard deviation (n)	15.3, 1.3, 33.5 (59)	13.4, 0.6, 40.8 (58)
Highest pre GAF, mean, median, standard deviation (n)	66.3, 65, 16.7 (79)	70.5, 72, 14.1 (69)
Baseline GAF, mean, median, standard deviation (n)	32.2, 35, 8.6 (79)	32.2, 32, 8.4 (71)
Only compulsory school, % (n)	21.5 (79)	26.8 (71)
Social support-limits in cooperation, % (n)	47.5 (80)	36.6 (71)
Significant alcohol consumption, % (n)	19 (79)	9.9 (71)
Working/studying half time or more, % (n)	46.8 (77)	62 (71)
Meets friends ≥2–3 times per month, % (n)	57.1 (77)	70.4 (71)
Motivated for treatment, % (n)	33.8 (80)	48.6 (72)
Lives with parents, % (n)	24.7 (81)	19.7 (71)
Married or cohabit with another person, % (n)	19.8 (81)	42.3* (71)
Previous psychiatric contact, % (n)	18.5 (81)	35.2* (71)

* $p < 0.05$.

psychoses with mood-incongruent delusions). In 120 of the patients it was possible to collect neuropsychological assessment data, using the Swedish version of the Wechsler Adult Intelligence Scale (WAIS-R) (Kaplan and Bartfai, 1994; Wechsler, 1994). The neuropsychological assessment was made within the first 3 months following admission in the vast majority of the patients (Carlsson et al., 2006). The highest GAF the year before first admission was estimated from information gathered from the patient and his/her relatives. Duration of untreated psychosis, DUP, was defined as the period between the first psychotic symptom and the first contact with psychiatric services and was counted in months. DUP was based on interviews with the patients and the relatives/network during the first week after admission. Most of the patients did not receive anti-psychotic medication during the first week (n = 108, 63%) which means that the time between entry into the study and initiation of such treatment is not included in the estimated DUP period (Cullberg et al., 2002).

The outcome measure

Flyckt et al. (2006) have provided a detailed description of the outcome. To assess outcome the psychiatric staff were repeatedly trained in the clinical assessment procedure in order to assure validity of the ratings. Clinical outcome was assessed during the fifth year after first admission. A poor outcome was defined as 'in need of continuous neuroleptic medication and support from professionals in everyday matters'. Such patients cannot work or study independently, require supported/sheltered jobs, or lead an inactive life. The GAF score should have been <60 for at least the last 6 months. A good outcome was defined as 'living a normal life' with or without neuroleptic medication and with no need for daily support from professionals'. The GAF score should have been stable ≥60 for at least 6 months and they should work or study independently at least half of the time. The cut-off level between poor and good outcome was set on an *a priori* basis. In cases close to this level the psychiatric personnel were instructed to pay special attention to work and social capacities to make the dichotomy robust and less sensitive to symptom fluctuations. Forty-four males and 24 females fulfilled the criteria of poor outcome and were compared with the remaining 37 males and 48 females with good outcome.

Predictive rating scale (PRS)

The PRS was developed from baseline characteristics, such as the level of functioning and symptoms of psychosis at baseline (Flyckt et al., 2006). The following measures were used: the BPRS, the age at first admission, the DUP, the highest GAF the year before admission, the baseline GAF, the highest educational level,

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the working/studying capacity, the frequency of meeting friends, 'lives with parents', married/cohabits/stable relationship and previous psychiatric contact. Furthermore the 'social network not capable of cooperation' was set by the staff if the network closest to the patient such as family and/or relatives had problems or was reluctant to cooperation or if there was no network. 'Not motivated for treatment' was set by the staff if the patient did not want to cooperate: that is, the patient could be under compulsory care and/or did not take the prescribed medication or did not want to stay in contact with the psychiatric team. 'Significant alcohol consumption' was based on interviews with the patients and the relatives/network and was set if the patient regularly consumed a corresponding amount of > one bottle of wine per week. All variables were dichotomized. No or mild symptoms (BPRS ≤ 2) were set at 'no symptoms' and moderate or severe symptoms (BPRS > 2) were set at 'symptoms'. The cut-off levels for the rest of the variables are presented in Table 2.

All patients did not answer all items which resulted in different dropout rates for the items. The number of respondents varied between 81 to 59 for males and 72 to 58 for females. Regarding the BPRS variables both males and females had the highest dropout in the items hopelessness/helplessness (males 67 and females 61 respondents) and somatic concern (males 70 and females 61 respondents). Regarding the dropout rates in the background/baseline variables DUP had the highest dropout rate both in males and in females (males 59 and females 58 respondents).

Only three females had a sum score of ≥4 among those with poor outcome. Gender differences in the predictive potential of the rating scale were assessed by comparing the distribution of males and females with a sum of risk factors ≥3 with those with a sum of risk factors <3 among patients with poor outcome (Figure 1). Two correlation matrices were performed, one with symptoms and one with background/functioning variables in order to examine if there were significant gender differences in the correlation coefficients (Tables 2 and 3). To examine predictors of outcome in males and females separately the same procedure was used as in the construction of the PRS but the analyses were divided gender-wise. A stepwise forward logistic regression analysis was performed including all variables except symptoms (Table 4).

Statistical analyses

All variables were summarized using standard descriptive statistics (e.g. mean, standard deviation and frequencies). The distributions of all variables were

Table 2. Relations between baseline variables and 5-year outcome. Gender differences in correlation coefficients (Pearson)

Characteristics	Males Pearson (*n*)	Females Pearson (*n*)	Equality of correlations males/females
Patient's age ≤25 years	0.045 (81)	0.388** (72)	<0.05
Duration of untreated psychosis ≥6 month	0.393** (59)	0.153 (58)	NS
Education level only compulsory school	−0.016 (79)	0.465** (71)	<0.01
Working/studying ≤ half time	0.242* (77)	0.264* (71)	NS
Lives with parents	−0.050 (81)	0.489** (71)	<0.001
Not married or cohabitant with another person	0.230* (81)	0.227 (71)	NS
Social network not capable of cooperation	0.129 (80)	0.099 (71)	NS
Meet friends ≤2–3 times a month	0.211 (77)	0.343** (71)	NS
Not motivated for treatment	−0.026 (80)	−0.138 (72)	NS
Highest GAF ≤70 the year before admission	0.311** (79)	0.321** (69)	NS
Current GAF ≤30	0.206 (79)	0.200 (71)	NS
Previous psychiatric contact(s)	−0.073 (81)	0.057 (71)	NS
Significant alcohol consumption	0.002 (79)	0.074 (71)	NS

Note: NS, not significant.
* $p < 0.05$, ** $p < 0.01$.

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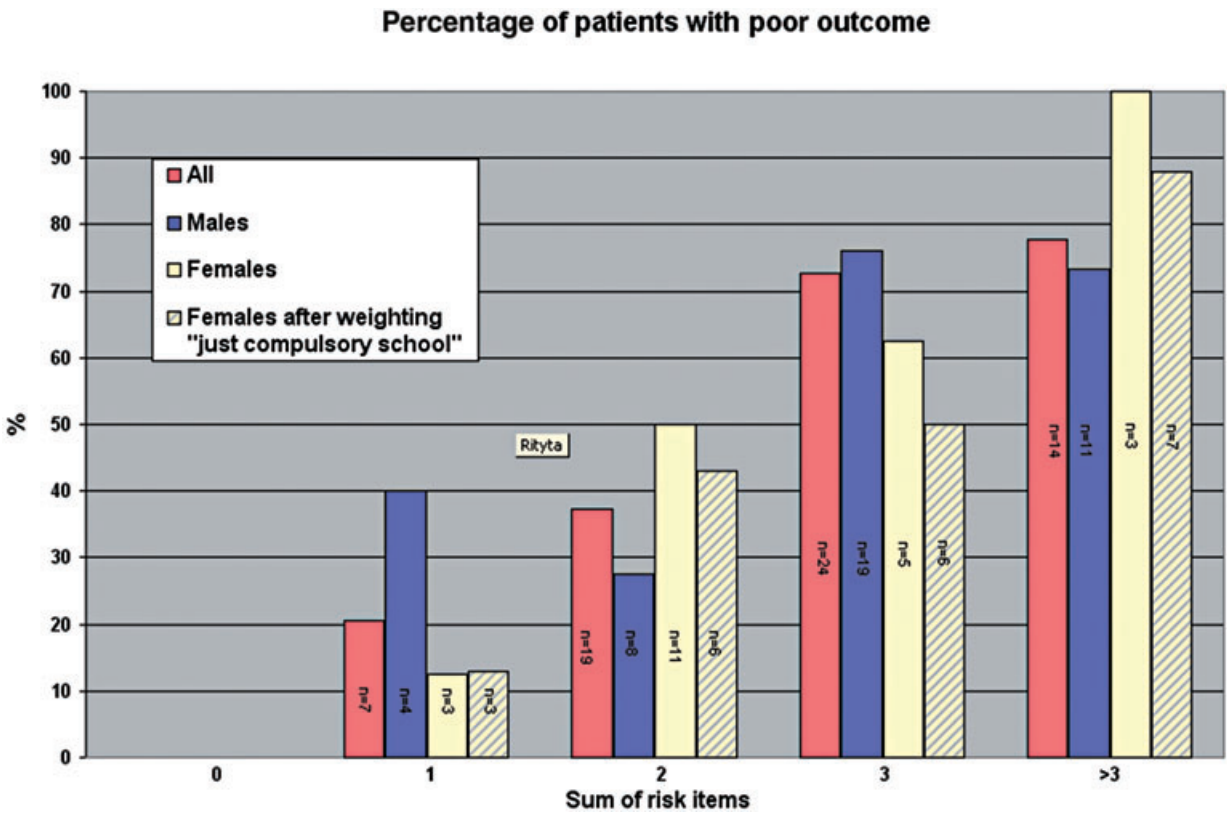

Figure 1. The percentage of patients, males ($n = 42$) and females ($n = 22$), with poor outcome for each sum of risk factors.

checked for skewed distributions and outliers. For skewed distribution non-parametric methods were applied. Most of the continuous baseline variables showed a skewed distribution and group differences were analysed using Mann–Whitney. Cognitive data were normally distributed and group differences were analysed with Student's t-test. Differences in frequencies for discrete variables were analysed with the Chi squared-test. Relationships between the dichotomized variables were expressed as Pearson's product moment correlation coefficients. Differences between groups in the correlation coefficients were checked by comparisons of correlation coefficients obtained by means of Fisher's z transformation. The unique contributions of the predictors to outcome were examined with stepwise forward logistic regression analyses. Statistical significance was set to $p < 0.05$ (two-tailed).

Results

Forty-two out of 44 of the males with poor outcome and 22 out of the 24 females with poor outcome had data on all five risk items in the PRS and were included in the comparison. Among females with poor outcome only three females had a score of ≥4 risk items. Eight females had a score ≥3 risk items therefore the comparison was made with a cut-off between two and three risk items. The sensitivity of the risk items was significantly better for males, 71.4% of the males with poor outcome had a score of ≥3 compared to 36.4% of the females (Chi squared = 7.369, $df = 1$, $p < 0.01$). Thus, the majority of females with a poor outcome were not correctly predicted by the PRS. For females the sensitivity was 36% and the specificity was 94%. The corresponding numbers for males were sensitivity 71% and specificity 73%. The percentage of male and female

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Table 3. Correlations between BPRS and 5-year outcome. Gender differences in correlation coefficients are also presented

BPRS symptoms	Males Pearson (*n*)	Females Pearson (*n*)	Equality of correlations males/females	BPRS symptoms	Males Pearson (*n*)	Females Pearson (*n*)	Equality of correlations males/females
Somatic concern	0.031 (70)	−0.162 (61)	NS	Disorientation	−0.155 (74)	−0.062 (65)	NS
Anxiety	−0.187 (72)	−0.201 (66)	NS	Conceptual disorganization	0.048 (74)	0.069 (67)	NS
Depression	−0.174 (71)	−0.157 (67)	NS	Blunted affect	0.197 (75)	0.198 (67)	NS
Suicidality	0.005 (72)	−0.110 (67)	NS	Emotional withdrawal	0.136 (75)	0.231 (67)	NS
Guilt	−0.238* (72)	−0.163 (64)	NS	Motor retardation	0.032 (75)	0.043 (67)	NS
Hostility	0.006 (73)	−0.168 (68)	NS	Tension	0.154 (75)	−0.258* (66)	<0.05
Elevated mood	0.089 (75)	−0.010 (67)	NS	Uncooperativeness	0.073 (75)	−0.007 (68)	NS
Grandiosity	0.092 (74)	−0.072 (66)	NS	Excitement	0.045 (75)	−0.006 (68)	NS
Suspiciousness	0.172 (74)	−0.104 (67)	NS	Distractibility	−0.057 (75)	−0.221 (66)	NS
Hallucinations	0.294* (71)	−0.032 (64)	NS	Motor hyperactivity	−0.001 (75)	−0.047 (67)	NS
Unusual thoughts	0.268* (72)	0.040 (64)	NS	Mannerism and posturing	0.089 (75)	−0.068 (68)	NS
Bizarre behaviour	0.257* (75)	0.116 (67)	NS	Hopelessness/helplessness	0.031 (67)	0.139 (61)	NS
Self neglect	−0.030 (73)	0.054 (67)	NS				

Note: NS, not significant.
*$p < 0.05$.

Table 4. Odds ratios for variables significantly ($p \leq 0.05$) contributing to the prediction of a poor outcome in male and female patients with first episode psychosis

	B	SE	P	OR	CI_{95}
Males – variables in the equation N = 54					
GAF year before admission ≤70	2.576	0.779	0.001	13.143	2.853–60.535
Current GAF ≤30	1.599	0.727	0.028	4.950	1.192–20.562
Constant	2.230	0.792			
Females – variables in the equation N = 57					
Compulsory school is the highest education level	2.638	0.860	0.002	13.983	2.592–75.435
Lives with parents	2.723	1.051	0.010	15.225	1.941–119.391
Meets friends <2–3 times per month	1.663	0.833	0.046	5.276	1.031–26.995
Constant	2.716	1.893			

Note: B, the slope of the regression line; SE, standard error of the B estimate; P, significance level; OR, odds ratio; CI_{95}, 95% confidence interval.

patients with poor outcome for each sum of risk factors (1–5) is shown in Figure 1.

To provide more detailed background information some of the baseline characteristics are presented as continuous variables (Table 1). The Mann–Witney test showed no differences in these background variables, however there were some differences between males and females in the dichotomous variables: a larger number of females than males were married/cohabiting/living in a stable relationship (Chi squared = 9.08, $df = 1$, $p < 0.01$) and had had a previous psychiatric contact (Chi squared = 5.44, $df = 1$, $p < 0.05$) (Table 1).

Two correlation matrices were performed to examine gender differences in the relations between background and baseline variables to outcome. First a correlation matrix was performed between symptoms at baseline and 5-year outcome for each gender. Equality of correlation was used to examine gender differences in the relation between symptoms and outcome. The results showed that there was a significant gender difference regarding the impact of the symptom tension at baseline on the 5-year outcome ($p < 0.05$) (Table 3).

Second, a correlation matrix was performed investigating the relationship between the 13 background variables, as defined in the method section and outcome for each gender (Table 2). These correlations also showed gender differences. Equality of correlation showed significant gender differences for the following baseline variables: age ≤25 years at first admission ($p < 0.05$), the highest educational level is just compulsory school ($p < 0.01$) and lives with parents ($p < 0.001$).

The unique contribution of all 13 baseline variables to 5-year outcome was examined in two gender-wise divided, logistic regression analyses. In order to include the same variables and the same people as in the original conclusive analysis for the prognostic scale, symptoms were not included in the analysis. The results showed that among males 'DUP', 'being married/cohabitant', 'the highest GAF the year before admission' and 'the current GAF at first admission' all contributed to a poor outcome, but only two of the variables, 'the highest GAF the year before admission' and 'the current GAF at first admission' had unique contributions (Table 4). Among females 'the age at first admission', 'the highest education is just compulsory school', 'living with parents', 'being married/cohabitant', 'working/studying', 'contact with friends ≤2–3 times a month' and 'the highest GAF the year before admission' significantly contributed to poor outcome. However, only 'the highest education being compulsory school', 'living with parents' and 'contact with friends ≤2–3 times a month' had a unique contribution (Table 4).

Because of missing data in baseline characteristics only 67% (54/81) of the males and 79% (57/72) of the females were included in the logistic regression analysis. The most frequent missing data was DUP for both genders. To examine how this could have affected the results males and females with DUP data were compared to those with no DUP data, respectively, regarding the other baseline variables included in the logistic regression. The analyses showed no significant differences between the groups.

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To better understand the results the relation between the strongest predictor and neuropsychological test results and diagnosis were examined for each gender separately. Females with a highest educational level of 'just compulsory school' performed significantly worse in the WAIS-R Full Scale IQ ($p < 0.01$), Verbal IQ ($p < 0.001$) and Performance IQ ($p < 0.05$) than those with higher education. Among males there were no such differences. There were no relations between 'the highest GAF the year before admission' and WAIS-R either for males or females. Overall, there were no differences between the genders regarding WAIS-R results (Carlsson et al., 2006).

Significantly more males with a 'highest GAF the year before admission' ≤70 had a schizophrenia spectrum diagnosis at baseline. For females there were no such relations. When looking at the relation between a schizophrenia spectrum diagnosis at baseline and outcome there was a significant correlation for females ($r = 0.340$, $p < 0.001$) but not for males, although the difference between genders was not significant. The highest level of education being compulsory school was not related to diagnosis for neither males nor females. When comparing the distribution of males and females with a schizophrenia/non-schizophrenia diagnosis among those with poor outcome no differences were found since there was a significant difference between males and females among those with favourable outcome. Among those with a favourable outcome significantly more males than females had a schizophrenia syndrome diagnosis (Chi squared = 5.25, $df = 1$, $p < 0.05$).

Adapting PRS to females with FEP

To increase the sensitivity of the PRS among females the presence of the risk-factor 'just compulsory school' was given two points instead of one for females, meaning that both males and females could reach a maximum score of five. The significant gender difference in the number of individuals facing a poor outcome in the PRS disappeared because more females with poor outcome were now captured by the PRS.

Fifty-nine per cent of the females with poor outcome had a score of ≥3 compared to 71% of the males (Chi squared = 0.997, $df = 1$, $p = 0.318$.). After adapting the scale the sensitivity increased from 36% to 59% and the specificity decreased from 96% to 85% in females.

Another way of adapting the scale to females was to exchange the risk-item 'contact with friends' with the item 'living with parents' because the latter was the second most important predictor after 'just compulsory school' for females in the logistic regression analysis. However, this procedure only marginally increased the percentage of correctly predicted female cases from 36% in the original scale to 39% whereas the percentage of correctly predicted male cases with a poor outcome decreased from 71% to 57%.

Discussion

A new scale, the PRS, has recently been introduced with the aim of identifying FEP patients at risk of facing poor outcome. The PRS has several advantages: it consists of only five items, it is easy to use by the psychiatric staff in their first encounter with a FEP patient and it is not time-consuming. The PRS showed promising results in assessing those at a risk of an unfavourable outcome (Flyckt et al., 2006). It is well known that males and females differ regarding age at onset, clinical features and outcome of psychosis (Foerster et al., 1991; Hafner, 2003; Lindamer et al., 2003; Preston et al., 2002; Salokangas et al., 2003; Usall et al., 2003) but this has not been sufficiently taken into account by the predictive scales available today (Phillips, 1953; Stephens et al., 1997; Strauss and Carpenter, 1974; Vaillant, 1964). Therefore, we have considered it important to examine whether the PRS had an equally promising predictive potential for both genders.

The results showed that the PRS more accurately predicted poor outcome in males, by weighting the risk item that differed most between males and females ('just compulsory school') the scale's predictive power increased for females and equalled that of males. The 'educational' item was the best predictor of a poor outcome for females whereas the best predictor for men was a low pre-admission level of functioning (the highest GAF the year before first admission ≤70). After the adaptation the number of females with poor outcome having ≥3 items increased from 8 to 13 which meant that the sensitivity increased from 36% to 59% and that the specificity decreased from 96% to 85%. In males the sensitivity was 71% and the specificity 73%. We think that this decline in specificity among females is of minor clinical importance. It is more important to capture more females at risk of poor outcome even if the number of false positives females also increases some and the specificity is still higher than for males. Other attempts to adapt the PRS to females proved to be less successful. If, for instance, the item 'contact with

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friends' was exchanged with 'living with parents' (the second best predictor for females) the predictive properties of the scale marginally increased for women but notably decreased for males. Another adaptation would be to construct different scales for males and females based on the order of odds ratios for each gender, but this would result in fewer items and would probably affect the stability of the scale. Thus, we found that the most accurate adaptation of the scale to the findings of gender differences in risk factors of a poor outcome was to maintain the original five-item PRS-scale and render the educational item a score of two for females. In this way the feasible aspect of the scale was maintained. However, these results must be confirmed by examining other FEP populations and by comparing them according to these results. Possible advantages of developing gender specific assessment tools must also be considered.

The results showed that there were gender differences regarding the relationships between the following baseline variables: the symptom 'tension', age at onset, education, 'living with parents' and long-term outcome. Certain predictors (education, 'living with parents' and 'contact with friends') were more specific for females while others were more valid for males ('the highest GAF the year before admission' and 'current GAF'). Although it is well known that females more often have a better pre-morbid functioning than males (Foerster et al., 1991; Hafner, 2003; Lindamer et al., 2003; Preston et al., 2002; Salokangas et al., 2003; Usall et al., 2003) it was somewhat unexpected that the highest GAF the year before admission did not contribute to explaining outcome among females being the strongest predictor among males. Previous studies have shown that the level of functioning before onset together with DUP have been the two most important predictors for poor outcome (Drake et al., 2000; Harrigan et al., 2003; Larsen et al., 2000; Malla et al., 2002; Marshall et al., 2005; McGorry et al., 2000; Norman et al., 2005; Perkins et al., 2005). In this study a significant relation between longer DUP and unfavourable outcome was found only among males although DUP did not make a unique contribution to outcome. The difference between males and females was not significant. DUP as a predictor of outcome has been widely discussed during the past decade. Some studies have concluded that DUP is a entity of its own while others have discussed whether DUP might be an epiphenomenon of pre-morbid functioning (Drake et al., 2000; Harrigan et al., 2003; Larsen et al., 2000; Malla et al., 2002; Marshall et al., 2005; McGorry et al., 2000; Norman et al., 2005; Perkins et al., 2005). This study provides some support for the latter view since, for males, there was a significant relation between longer DUP and unfavourable outcome although DUP alone did not make a unique contribution to outcome. Consequently, there may be a reason to believe that a poor pre-morbid functioning, the strongest predictor of poor outcome among males, may be a denominator behind the relationship between a long DUP and pre-morbid functioning.

However the logistic regression analysis included only 67% of the males and 79% of the females. For both genders the most frequent missing data was DUP. Comparisons between males and females with and without DUP data showed no significant differences between the groups but this might be due to low power. The possibility that the high missing data rate might have affected the result cannot be excluded.

The relation between a diagnosis of schizophrenia spectrum disorder and poor outcome was stronger among females than males although the difference was not significant. For patients with poor outcome there were no gender differences in the frequencies of schizophrenia spectrum diagnoses, the distribution was almost equal for males and females, however, for patients with favourable outcome there were more males than females with a schizophrenia syndrome diagnosis in spite of the fact that males with a poor pre-morbid functioning, measured with 'the highest GAF the year before first admission', more often had a schizophrenia syndrome diagnosis than females. These results might indicate that diagnosis is not an optimal predictor due to the gender differences and previous research has also found that psychosis diagnoses show instability over time (Rahm and Cullberg, 2006).

Due to missing data WAIS-R results were not entered into the logistic regression analysis. In other studies, cognitive impairment can be a strong predictor of unfavourable outcome in patients with psychosis (Carlsson et al., 2006). In Sweden approximately 98% of all young people continue with further studies after compulsory school and there is no difference between the genders. Our sample reflects the population since there was no gender difference in this respect (Table 1). We found that a low educational level was the primary predictor of unfavourable outcome in the females, but not in the males (Table 4). Females with only compulsory school also performed worse than females with higher

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education, but that difference was not seen in the males. Other studies and reports based on our data (Carlsson et al., 2006) have shown that cognitive function was a strong predictor of outcome. The present results may suggest that cognitive function explains this finding among the females. PRS may be used to identify those patients where a comprehensive neuropsychological examination can further strengthen the predictive power, and to suggest the most effective treatments.

In this study we have not taken into account the possible confounding effect of the treatment on outcome. The need-adapted treatment may alter the outcome for the included patients and therefore restrict the generalizability of the results but, since the treatment may ameliorate outcome (Cullberg et al., 2002), a possible alteration should be applicable to those patients with a favourable outcome and not those with a poor one. More studies in this field are needed to increase the knowledge in how treatment factors can relate to gender specific risk factors. Furthermore, this study has not taken into account the possible effect of weighting the items included in the PRS according to the odds ratios in the regression model which the PRS is based on.

There were two main limitations of this study, i.e. a low power and an unsatisfactory sensitivity. The effect of a low power is that the possibility of detecting a significant effect is decreased. Such a low number of degrees of freedom allows us to detect only large effect sized coefficient ($r = 0.50$) with a sufficient power (power ≥ 0.85, $p = 0.05$) but moderate correlations ($r = 0.30$) with a insufficient power, or less than 0.80 for both the male and the female sample. To decrease the power further by applying corrections for multiple comparisons (e.g. Tukey's HSD or Bonferroni) could thus not be justified.

The second limitation is the modest sensitivity, 0.59 for females and 0.71 for males. Such a low sensitivity restricts the clinical applicability of our results. In a planned study, we will include a larger sample of patients and other variables probably contributing to the explanation of outcome (e.g. cognitive functions, insight into illness). In this way, we expect to contribute to an increased sensitivity as well as specificity of the PRS.

The gender differences in the prediction of outcome for FEP patients may be attributed to gender differences in specific domains such as sociability, the ability to work/study, ability in all daily life matters and symptom severity. This needs to be examined in future studies. The results in this study indicate that when the impact of various determinants of outcome among FEP patients are examined, it is of importance that males and females are analysed separately (Larsen et al., 2000) as this might lead to the development of intervention programmes with diversified care for males and females.

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