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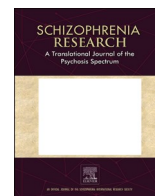
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Sex differences and age of onset in well-being and recovery in people with psychotic disorders. A PHAMOUS study

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ABSTRACT

Purpose: Women generally have a later age of onset, and may therefore have a more favourable course of psychotic illness than men regarding psychopathology. Little is known about a broader range of outcomes, including well-being and recovery, and about the influence of age of onset. This study examines longitudinal sex-related and age of onset-related differences in well-being and recovery of people with a psychotic disorder with long illness durations.

Methods: Routine outcome monitoring data (2012–2021) of $n = 3843$ patients were used. Well-being (quality of life and personal recovery) and recovery (clinical and societal recovery and psychosocial functioning) were assessed. Latent class growth analysis (LCGA) was performed to assess whether classes with different trajectories of well-being and recovery could be identified. Classes were related to sex and (early/late) age of onset of psychosis (EOP/LOP).

Results: LCGA identified five classes with varying combinations in levels of well-being and recovery, which were stable over time. Sex, age of onset and the combination of these two were significantly related to class membership. Women and individuals with LOP were more prevalent in better functioning classes than men and individuals with EOP.

Conclusion: This study showed sex differences in long-term recovery patterns of psychosis. Not only women but also individuals with LOP had a higher chance of better well-being and recovery, while men with EOP were at risk for worse outcomes. Taking these sex differences into account when deciding on policy and treatment protocols for individual patients might provide better mental health care to people with psychosis.

1. Introduction

Psychotic disorders appear to affect men and women differently. Women with psychotic disorders seem to have less interrupted lives and better outcomes than men (Albert et al., 2011; Castelein et al., 2021; Riecher-Rössler et al., 2018). For example, women typically have a three to five year later onset and less severe psychopathology, which is associated with shorter hospital stays and the need for lower doses of antipsychotics than men (Leung and Chue, 2000; Rabinowitz et al., 2006; Riecher-Rössler et al., 2018). Furthermore, treatment compliance, treatment response and illness insight appear to be better in women than in men (Cotton et al., 2009; Thorup et al., 2014). Men are more likely to

be unemployed and to live alone after a first episode of psychosis (Carter et al., 2022; Thorup et al., 2007, 2014).

Unfortunately, knowledge regarding sex differences in psychosis is often based on small and non-representative samples (Riecher-Rössler et al., 2018). Furthermore, most research regarding sex-differences in psychosis has focused on the course and outcome of clinical symptoms, rather than the broad range of domains that is affected by psychosis. However, it can be hypothesized that women with psychotic disorders also have a more favourable course and outcome in other areas of recovery (personal recovery, societal recovery), psychosocial functioning and quality of life. One reason for this could be the relatively higher age of onset that may have a protective effect (da Silva and Ravindran, 2015; Ochoa

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et al., 2012), since women are therefore likely to have more stability in life, with a completed education, a job, a partner, and stable social networks (Riecher-Rössler and Häfner, 2000; Sawicka et al., 2013; Thorup et al., 2007), which is predictive of greater well-being (Proctor et al., 2023).

Moreover, men and women (are expected to) behave differently based on gender roles, which may impact the course of well-being and recovery as well, for example through different expressions of their well-being, different societal roles, and dealing with gender stereotypes (Blakemore et al., 2008). These gender roles generally evolve with age (Blakemore et al., 2008) and tend to influence how psychosis affects people's lives, with men more often experiencing loss in terms of work and women more often experiencing loss in terms of parenting (Firmin et al., 2021). The age of onset of psychosis may therefore be a factor of importance, when looking at sex differences in the course of well-being and recovery in psychosis.

Age of onset is categorized as early onset of psychosis (EOP), defined as the first psychotic episode occurring before or at the age of 40 years, and late onset of psychosis (LOP), defined as the first episode occurring at 41 years or older (Howard et al., 2000), with women more often than men having a LOP (Riecher-Rössler et al., 2018). There are some indications that age of onset might affect the course of well-being and recovery in people with psychosis. People with LOP tend to have more stability in life, which would make a more favourable course and outcome of well-being and recovery more likely (Riecher-Rössler and Häfner, 2000). Among women, one study found a better quality of life, lower self-stigma and less antidepressant use in women with EOP compared to LOP (Dubreucq et al., 2021). Unfortunately, there is a general underrepresentation of women in psychosis literature (Carter et al., 2022), and women with late onset psychosis are particularly often overlooked (Ochoa et al., 2012), since many studies use age limits between 35 and 45 years old (Carter et al., 2022; Riecher-Rössler et al., 2018). Therefore, the role of age of onset and its interaction with sex differences remains unclear in regard to the course of well-being and recovery of people with psychotic disorders.

Since both sex and age of onset might influence the course of various well-being and recovery outcomes in psychosis, researching these factors is highly relevant for clinical practice. Therefore, the aim of this study is to examine sex-related differences in the course of well-being and recovery, in a sample of people with psychotic disorder with a long illness duration (average of 15 years). Furthermore, we will explore whether age of onset of psychosis is a factor of importance in the course of these outcomes.

2. Methods

2.1. Study design

Routine outcome monitoring data from the Pharmacotherapy Monitoring and Outcome Survey (PHAMOUS) were used (Bartels-Velthuis et al., 2018). PHAMOUS is a large, annual screening for patients with a psychotic disorder and/or people using antipsychotic medication receiving care from several mental health institutions in the Northern Netherlands. For this study, patients from three different mental health institutions specialized in severe mental illness (Lentis Psychiatric Institute $n = 6830$; GGZ Friesland Mental Health Institute $n = 8675$; GGZ Drenthe Mental Health Institute $n = 3901$) and one psychiatric hospital (University Centre for Psychiatry $n = 991$) participated. PHAMOUS-screenings are done face-to-face by trained nurses. Screenings are part of regular care and include assessments of mental, physical and social domains. Based on these screenings a report is written and a treatment plan is developed. Patients can opt out for the use of their data for scientific research. Since the anonymized data was received through a third party, there is no way of knowing how many patients opted out for the research. Research on these data was omitted from the Medical Research Involving Human Subjects Act (WMO) by the Medical Ethical Committee of the University Medical Center Groningen (METc 2015/347), which is in accordance with the Declaration of the Helsinki (World Medical Association, 2013). The exemption was provided, because PHAMOUS screenings are part of regular care and therefore

do not add additional burden to patients.

2.2. Sample

Individuals with PHAMOUS-screenings between 2012 and 2021 and a diagnosis on the psychotic spectrum (DSM-IV or DSM-V) were included (American Psychiatric Association, 2013; American Psychiatric Association, 2000). Patients were included if they were ≥ 18 years and had data available on sex, age of onset and at least one of the outcomes (quality of life, personal recovery, clinical recovery, societal recovery or psychosocial functioning) on at least one assessment.

2.3. Measurements

Participants completed demographic questions with regard to biological sex, age, age of onset of psychosis and living situation.

2.3.1. Assessment of well-being

Well-being was operationalized as experienced quality of life and personal recovery.

Quality of life was assessed using the Manchester Short Assessment of Quality of Life (ManSA; Priebe et al., 1999). The ManSA is a 16-item self-report questionnaire including four yes/no items and twelve items on a 7-point Likert scale, with higher scores representing greater quality of life. For this study, the 12-Likert scale items are used. The ManSA-score is the sum of the item scores (range: 12–84).

Personal recovery was examined with a proxy, using the single-item Happiness Index (HI; Abdel-Khalek, 2006). Participants were asked to rate how happy they were in the last month on a scale of 1–10, with a higher score indicating more happiness, symbolizing greater personal recovery.

2.3.2. Assessment of recovery

Recovery was operationalized as clinical recovery, societal recovery and psychosocial functioning.

Clinical recovery (i.e. symptomatic recovery) was measured using the Positive and Negative Syndrome Scale (PANSS). This semi-structured interview measures the severity of psychotic symptoms in the past week (Kay et al., 1987). The PANSS consists of 30 items scored on a 7-point Likert scale. The PANSS-score is the sum of the item scores, with lower scores representing greater clinical recovery (range: 30–210).

Societal recovery was measured using the Functional Recovery Tool (FRT; Swildens et al., 2018). This semi-structured interview addresses three domains of functioning in the past six months: 1) daily living and self-care, 2) work, study and housekeeping, and 3) social contacts. These domains are rated on a 3-point Likert scale. The FRT-score is the sum of the item scores (range: 0–6), with lower scores representing better societal recovery.

Psychosocial functioning was measured using the Health of the Nation Outcome Scales (HoNOS; Wing et al., 1998). The HoNOS is a 12-item clinician-rated questionnaire, assessing problematic behaviour and symptoms in the past two weeks on a 5-point Likert scale. The HoNOS-score is the sum of the item scores (range: 0–48), with a higher score indicating more problematic behaviour.

2.4. Data analysis

Descriptive analyses were used to compare patient characteristics between men and women at first assessment (using SPSS, version 26). Differences between men and women were compared using chi-square tests (EOP or LOP, type of diagnoses, living situation) and independent *t*-tests (age, age of onset, illness duration, ManSA, HI, PANSS, FRT and HoNOS). Latent class growth analysis (LCGA; Nagin, 1999) was performed to assess whether classes with different trajectories of well-being and recovery could be identified (using Latent GOLD, version 6.0). LCGA is a statistical approach in which individuals with similar longitudinal patterns over time (i.e., trajectories) on the outcome variables are grouped together into a

class, and in which individuals with clearly different patterns belong to different classes. Individuals were grouped based on their scores on the ManSA (treated as continuous in the LCGA), HI (treated as ordered categorical, 10 categories), PANSS (continuous), FRT (categorical, 7 categories) and HoNOS (continuous). Each individual trajectory per outcome variable was modelled with an intercept, expressing the level at first assessment, and a linear effect of time (in months), expressing the general trend across time. We fitted three types of models; model A) with intercept, slope and residual variances (of continuous variables) class dependent; B) with intercept and residual variances class dependent; and C) with intercept class dependent. The models were fitted using all available data, thereby assuming missing data was missing at random. The HoNOS had the least missing data (23 %) throughout the assessments, and the FRT had the most missing data (52 %) throughout the assessments (please see Table 1, supplementary material). We determined the type of model and the number of classes first based on the statistical Bayesian information criterion (BIC), subsequently checking its interpretability. The BIC is a widely accepted index for latent categorical variable models (Lanza et al., 2007). Specifically, we fitted the three types of LCGA models with the number of classes from one to ten. We selected the final model as having the lowest BIC value, or if not attained for a nine class solution, the one for which the

BIC value levels off and shows good interpretability. Subsequently, we used regression of the classes on sex, age of onset, the interaction between sex and age of onset, and illness duration taking into account the uncertainty owing to the estimation of the class memberships (i.e., the class membership of each individual is expressed in terms of probabilities, for example 0.1 [Class 1], 0.2 [Class 3], 0.7 [Class 4]) (Bakk et al., 2013). These were exploratory tested with the chi-squared test ($\alpha = 0.01$), with Bonferroni correction for multiple testing with four tests, meaning significance was tested against $\alpha = 0.0025$.

3. Results

In total, $n = 3843$ patients were included in the analyses with a minimum of two and a maximum of twelve screenings (see Table 1). Living situation differed significantly between sexes ($p < 0.01$), with women more often living with a partner and/or children and men more often living sheltered or with other family. Women showed significantly ($p < 0.01$) better ManSA, PANSS, FRT and HoNOS-outcomes. Personal recovery did not differ significantly between sexes. The majority of the sample were men with EOP (59.2 %), followed by women with EOP (28.9 %), women with LOP (6.2 %) and men with LOP (5.6 %). On

Table 1
Demographic characteristics of sample (at first assessment).

	Total sample	Men			Women			95%CI ^a
		Total	EOP	LOP	Total	EOP	LOP	
Number of screenings, M (SD)	3.4 (2.1)	3.4 (2.1)	3.4 (2.1)	3.1 (2)	3.4 (2.1)	3.4 (2.1)	3.1 (2)	-0.02 to 0.11
Sex, n (%)		2493 (64.9)			1350 (35.1)			
Current age, M (SD)	43.6 (11.7)	42.4 (11.6)	41.2 (11.3)	55.0 (6.4)	46.0 (11.6)	44.0 (11.5)	55.3 (6.6)	-1.5 to -0.03*
Age of onset								
Years, M (SD)	27.2 (10.1)	26.2 (9.3)	24.2 (6.6)	47.5 (5.3)	29.1 (11.3)	25.0 (7.2)	48.1 (6.2)	-3.5 to -2.2***
Early onset, n (%)	3387 (88.1)	2276 (91.3)			1111 (82.3)			0.07 to 0.12**
Late onset, n (%)	456 (11.9)	217 (8.7)			239 (17.7)			-0.15 to -0.03**
Illness duration, M (SD)	14.8 (11.2)	14.6 (11)	15.4 (11.1)	6.0 (5.5)	15.3 (11.5)	17.4 (11.4)	5.8 (5.6)	-1.5 to -0.04*
Type of diagnosis								
Schizophrenia, n (%)	2162 (56.3)	1566 (62.8)	1475 (64.8)	91 (41.9)	596 (44.1)	505 (45.5)	91 (38.1)	0.14 to 0.23**
Schizoaffective disorder, n (%)	604 (15.7)	291 (11.7)	272 (12)	19 (8.8)	313 (23.2)	285 (25.7)	28 (11.7)	-0.17 to -0.06**
Schizophreniform disorder, n (%)	86 (2.2)	59 (2.4)	55 (2.4)	4 (1.8)	27 (2.0)	27 (2.4)	0	-0.06 to 0.07
Substance induced psychotic disorder, n (%)	66 (1.7)	52 (2.1)	45 (2.0)	7 (3.2)	14 (1.0)	10 (0.9)	4 (1.7)	-0.05 to 0.08
Delusional disorder, n (%)	130 (3.4)	76 (3.0)	54 (2.4)	22 (10.1)	54 (4.0)	32 (2.9)	22 (9.2)	-0.07 to 0.05
Other/unspecified, n (%)	841 (21.9)	481 (19.3)	405 (17.8)	76 (35)	360 (26.7)	263 (23.7)	97 (40.6)	-0.13 to -0.02**
Living situation ^b								
Independent, alone, n (%) ^c	1342 (34.9)	851 (34.1)	766 (33.7)	85 (39.2)	491 (36.4)	381 (34.3)	110 (46)	-0.08 to 0.03
Independent, with partner and/or children, n (%) ^d	441 (11.5)	193 (7.7)	156 (6.9)	37 (17.1)	248 (18.4)	178 (16)	70 (29.3)	-0.17 to -0.05**
With other family (e.g. parents), n (%) ^e	333 (8.7)	251 (10.1)	238 (10.5)	13 (6)	82 (6.1)	75 (6.8)	7 (2.9)	0.00 to 0.1**
Sheltered, n (%) ^f	745 (19.4)	536 (21.5)	480 (21.1)	56 (25.8)	209 (15.5)	184 (16.6)	25 (10.5)	0.00 to 0.12**
Well-being outcomes								
ManSA, M (SD)	58.3 (12.1)	57.6 (12.2)	57.7 (12.1)	55.7 (12.5)	59.8 (12.0)	59.9 (12.0)	59.2 (12.2)	-3.2 to -1.2***
HI, M (SD)	6.4 (1.8)	6.4 (1.8)	6.4 (1.7)	6.1 (1.8)	6.5 (1.9)	6.5 (1.9)	6.2 (1.8)	-0.23 to 0.05
Recovery outcomes								
PANSS, M (SD)	51.9 (15.9)	53.1 (16.3)	53.4 (16.4)	50.0 (14.3)	49.5 (14.9)	49.5 (15.1)	49.6 (14.3)	2.1 to 5.2***
FRT, M (SD)	2.6 (1.7)	2.8 (1.7)	2.8 (1.7)	2.5 (1.8)	2.2 (1.7)	2.3 (1.7)	1.9 (1.6)	0.36 to 0.73***
HoNOS, M (SD)	10.1 (6.2)	10.4 (6.3)	10.4 (6.3)	10.6 (6.2)	9.4 (5.9)	9.4 (6.0)	9.0 (5.3)	0.6 to 1.6***

Note. M = mean; SD = standard deviation; ManSA = Manchester Short Assessment of Quality of Life; HI = Happiness Index; PANSS = Positive and Negative Syndrome Scale; FRT = Functional Recovery Tool; HoNOS = Health of the Nation Outcome Scales.

^a 95 % confidence interval for *t*-test or chi-square test for differences between men and women, with * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

^b Living situation: 145 individuals (3.8 %) had a living situation defined as 'other'.

^c 'Independent, alone' refers to individuals living independent, this also includes individuals living independent with a roommate.

^d 'Independent, with partner and/or children' refers to individuals living independent who have a partner and/or (dependent) children.

^e 'With other family (e.g. parents)' refers to a dependent form of living situation.

^f 'Sheltered' refers to individuals living in a form of supported housing or in long term clinical care.

average, women had a three year later age of onset than men ($p < 0.01$).

3.1. Five latent classes of well-being and recovery

We selected model B, with class dependent intercept and residual variances, because its BIC was lower for each number of classes than the BIC of the other two competitor models. For model B, we selected the model with five latent classes, because the lowest BIC was not attained for the nine class solution, and the BIC levels off at five classes (see Table 2). Also, this model had a good interpretability. The average class probabilities were high for all five classes (0.85–0.91), suggesting that participants were generally adequately assigned to their classes.

3.2. Description of the five well-being and recovery classes

In the selected model B, the effect of time is significant (except for FRT), but its size is very small compared to the differences in intercepts between the classes. Further, the effect of time is constant across classes. Therefore, in interpreting the selected model, we focused on the differences in intercepts between the classes. We ordered the classes in terms of well-being outcomes, i.e. from better to worse ManSA and HI-scores. In Table 2 of the supplementary materials, the estimated model parameters are presented.

To allow for an easy comparison between classes, Table 3 shows per class the estimated mean (and SD), with statistical test results. The estimated means are presented across all measurements, in view of the very small and class independent time effects, meaning that the little change over time on the outcome variables is the same across classes.

Class 1 had the most favourable pattern, with good scores on all five well-being and recovery outcomes. Good well-being is demonstrated by the $M = 68.1$ score on quality of life (ManSA) and $M = 7.6$ on personal recovery (HI). Clinical recovery (PANSS; $M = 37.8$) can be interpreted as on the threshold for mentally ill (Leucht et al., 2005). Class 1 showed good societal recovery (FRT $M = 1.2$) and psychosocial functioning (HoNOS $M = 4.3$). We refer to Class 1 as ‘good well-being, good recovery’.

Class 2 had similar well-being outcomes, but worse recovery outcomes compared to Class 1. Good well-being is demonstrated by the ManSA ($M = 67.6$) and HI ($M = 7.7$) scores. Clinical recovery (PANSS; $M = 52.3$) was interpreted as mildly ill (Leucht et al., 2005). Class 2 showed sufficient societal recovery (FRT $M = 3.5$) and psychosocial functioning (HoNOS $M = 4.3$). We refer to Class 2 as ‘good well-being, sufficient recovery’.

Class 3 had a somewhat in-between pattern, with worse well-being outcomes than Class 1 and 2, but better than Class 4 and 5, and only slightly worse recovery outcomes than Class 1. Well-being in Class 3 was medium, which is demonstrated by the ManSA ($M = 57.9$) and HI ($M = 6.5$) scores. Clinical recovery (PANSS; $M = 44.8$) was interpreted as on the

threshold for mentally ill (Leucht et al., 2005). Class 3 showed good societal recovery (FRT $M = 1.8$) and psychosocial functioning (HoNOS $M = 7.0$). We refer to Class 3 as ‘moderate well-being, good recovery’.

Class 4 and 5 had the least favourable outcome patterns. Class 4 had the worst recovery scores of the five classes, but better well-being scores than Class 5, albeit still in the lower ranges. Well-being in Class 4 was just sufficient (ManSA: $M = 53.7$; HI: $M = 5.9$). Clinical recovery (PANSS; $M = 69.6$) was interpreted moderately ill (Leucht et al., 2005). Class 4 showed insufficient societal recovery (FRT $M = 4.7$) and sufficient psychosocial functioning (HoNOS $M = 16.2$). We refer to Class 4 as ‘sufficient well-being, insufficient recovery’.

Class 5 had the lowest well-being scores, but recovery scores that were somewhat similar to Class 2. Insufficient well-being is demonstrated by the ManSA ($M = 49.8$) and HI ($M = 5.4$) scores. Clinical recovery (PANSS; $M = 54.7$) was interpreted as mildly ill (Leucht et al., 2005). Class 5 showed sufficient societal recovery (FRT $M = 2.7$) and psychosocial functioning (HoNOS $M = 10.6$). We refer to Class 5 as ‘insufficient well-being, sufficient recovery’.

3.3. Class differences regarding sex and age of onset

The five identified classes of well-being and recovery were compared on sex and age of onset (see Table 4 for summary statistics across all measurements; $n = 3843$ patients with a total of $n = 18,212$ measurements), and on illness duration. Sex ($W = 285.4$; $p < 0.01$) is significantly related to class membership, with more women in the better functioning Class 1 (‘Good well-being, good recovery’) and more men in the worse functioning Class 4 (‘Sufficient well-being, insufficient recovery’) and Class 5 (‘Insufficient well-being, sufficient recovery’). Age of onset ($W = 46.4$; $p < 0.01$) is significantly related to class membership, with EOP having a stronger presence in the worse functioning Class 4 (‘Sufficient well-being, insufficient recovery’), and EOP and LOP having similar distributions across the other classes. The combination of sex and age of onset ($W = 180$; $p < 0.01$) showed that women with LOP were most often assigned to better functioning classes Class 1 and 2 (‘Good well-being, good recovery’ and ‘Good well-being, sufficient recovery’, respectively), followed by men with LOP and women with EOP. A reversed pattern is seen in the worse functioning Class 4 (‘Sufficient well-being, insufficient recovery’), which has predominantly men with EOP. Lastly, illness duration ($W = 680$; $p < 0.01$) was significantly related to class membership, where people with a shorter illness duration were more often assigned to better functioning classes.

4. Discussion

This study examined sex-related differences in well-being and recovery of people with a generally long duration of psychotic disorders ($M = 14.8$

Table 2
Fit indices for LCGA.

Model	Model A			Model B			Model C			
	n_class ^a	n_para ^b	LL ^c	BIC ^d	n_para ^b	LL ^c	BIC ^d	n_para ^b	LL ^c	BIC ^d
1	27		-173,810	347,843	27	-173,810	347,843	27	-173,810	347,843
2	40		-167,249	334,828	35	-167,271	334,831	32	-168,381	337,026
3	53		-165,258	330,953	43	-165,275	330,905	37	-166,417	333,139
4	66		-163,565	327,675	51	-163,592	327,604	42	-164,998	330,343
5	79		-162,752	326,157	59	-162,781	326,048	47	-164,236	328,861
6	92		-162,217	325,193	67	-162,244	325,041	52	-163,691	327,811
7	105		-161,750	324,367	75	-161,780	324,179	57	-163,302	327,074
8	118		-161,405	323,785	83	-161,445	323,574	62	-163,029	326,569
9	131		-161,078	323,237	91	-161,118	322,986	67	-162,792	326,138
10	144		-160,841	322,871	99	-160,892	322,601	72	-162,569	325,732

Note. Model A. class dependent intercept, slope and residual variances; model B. class dependent intercept and residual variances; model C. class dependent intercept. Selected model is indicated in bold face.

^a Number of classes.

^b Number of parameters.

^c Log likelihood.

^d Bayesian Information Criterion.

Table 3
Descriptive results for outcome measures across all measurements.

	Total sample	Class 1 'Good well-being, good recovery'	Class 2 'Good well-being, sufficient recovery'	Class 3 'Moderate well-being, good recovery'	Class 4 'Sufficient well-being, insufficient recovery'	Class 5 'Insufficient well-being, sufficient recovery'
N (% of sample)	3843	760 (19.8 %)	758 (19.7 %)	915 (23.8 %)	577 (15 %)	833 (21.7 %)
Well-being						
ManSA, M (SD)	59.4 (11.8)	68.1 (7.3) ^{*3,4,5}	67.6 (9.1) ^{*3,4,5}	57.9 (8.3) ^{*1,2,4,5}	53.7 (11.7) ^{*1,2,3,5}	49.8 (10.4) ^{*1,2,3,4}
HI, M (SD)	6.6 (1.6)	7.6 (1.1) ^{*3,4,5}	7.7 (1.1) ^{*3,4,5}	6.5 (1.3) ^{*1,2,4,5}	5.9 (1.6) ^{*1,2,3,5}	5.4 (1.6) ^{*1,2,3,4}
Recovery						
PANSS, M (SD)	51.8 (15.6)	37.8 (6.7) ^{*2,3,4,5}	52.3 (13.3) ^{*1,3,4,5}	44.8 (9.2) ^{*1,2,4,5}	69.6 (18.0) ^{*1,2,3,5}	54.7 (12.8) ^{*1,2,3,4}
FRT, M (SD)	2.8 (1.8)	1.2 (1.1) ^{*2,3,4,5}	3.5 (1.3) ^{*1,3,4,5}	1.8 (1.3) ^{*1,2,4,5}	4.7 (1.1) ^{*1,2,3,5}	2.7 (1.4) ^{*1,2,3,4}
HoNOS, M (SD)	9.6 (5.9)	4.3 (2.9) ^{*2,3,4,5}	10.2 (5.1) ^{*1,3,4}	7.0 (3.6) ^{*1,2,4,5}	16.2 (6.2) ^{*1,2,3,5}	10.6 (4.5) ^{*1,3,4}

Note. M = mean; SD = standard deviation.

* Significantly different at $\alpha = 0.01$ from scores in other classes (e.g. Class 1 ManSA^{*3,4,5} indicates ManSA-scores of the first class are significantly different from ManSA-scores in the third, fourth and fifth class).

Table 4
Sex and age of onset groups per class across all measurements.

	Total sample, 100 %	Men, %	Women, %	EOP, %	LOP, %	Men, EOP, %	Women, EOP, %	Men, LOP, %	Women, LOP, %
Class 1	17.3	14.7	22.2	19.3	19.4	15.7	18.6	21.6	24.5
Class 2	20.7	20.8	20.5	19.7	21.8	20.1	21.4	22.3	22.8
Class 3	23.9	23.0	25.7	23.3	24.0	23.4	24.5	25.1	25.2
Class 4	16.4	19.2	11.1	16.1	11.5	19.2	13.7	9.5	6.5
Class 5	21.7	22.4	20.5	21.5	23.3	21.8	21.9	21.6	21.0
Total, n	18,212	11,892	6320	16,315	1897	10,975	5340	917	980

Note. Notable sex differences within a class of 5 % or more are highlighted (in bold), e.g. there are 7.5 % more women than men in Class 1.

years), taking age of onset into account. Women more often had a LOP, lived independently, had a better quality of life, clinical and societal recovery, and better psychosocial functioning than men. Personal recovery differs minimally between sexes. However, these comparisons across all assessments do neither examine how sex differences evolve over time, nor how the various outcome measures relate to each other. Therefore, we executed a LCGA, which identified five well-being and recovery classes, including two more favourable classes, two less favourable classes and one 'in-between pattern'. Classes were relatively stable over time with minimal change in outcomes. Sex, age of onset, their interaction effect and illness duration were significantly related to class membership. Women had a higher presence in better functioning classes (e.g. Class 1) than men. With regard to age of onset, our results showed that individuals with EOP were more likely to be in the worse functioning classes (e.g. Class 4). Women and individuals with LOP are thus more likely to have better outcomes. This was also connected to illness duration with LOP generally having shorter illness duration and people with a shorter illness duration being more frequently present in better functioning classes.

In line with our results, previous studies also found that female sex was a predictor of a more favourable course of illness (Albert et al., 2011; Cotton et al., 2009; Thorup et al., 2014), with women having better clinical and societal recovery in particular (Albert et al., 2011; Cotton et al., 2009; Poppe et al., 2024). A lack of sex differences in personal recovery is also previously reported, in the scarce study that addressed sex differences in personal recovery (Leendertse et al., 2021). Previous studies regarding quality of life in people with psychotic disorders, for which this study found better results in women than men, are ambiguous with one study finding better quality of life in men (Dubreucq et al., 2021), another in women (Caron et al., 2005), and a third finding no differences between men and women at all (Thorup et al., 2014).

Since literature regarding age of onset was scarce, we wanted to explore the effect of age of onset in relation to well-being and recovery. Our results suggest that not only women, but all individuals with LOP have a higher chance at better well-being and recovery. Earlier studies that addressed both factors also found female sex and a later age of onset to be predictive of better clinical and societal recovery (Albert et al.,

2011; Chang et al., 2018; Hodgekins et al., 2015; Thorup et al., 2014), but note that these studies only included patients up to 45 years old. Moreover, oestrogen is proposed to play a protective role in psychosis (da Silva and Ravindran, 2015). However, this might mainly apply to women with EOP, since it is suggested that changing oestrogen levels during menopause result in a worse course and outcome in women with LOP, compared to women with EOP (González-Rodríguez et al., 2020). This is in line with a study addressing a broader age range that only found a better societal recovery in women with an EOP, but not LOP in comparison with men, and a worse quality of life in women with a LOP as compared to women with an EOP (Dubreucq et al., 2021). Another study found better clinical recovery in women aged up to 65 years old and saw a less favourable outcome after this age (Köhler et al., 2009).

Better experienced well-being did not always coincide with better recovery. This might be partially explained by having self-report measures for well-being, but observer-rated measures for recovery. Furthermore, people's (gender) roles and identity are also affected by experiencing a psychosis (Firmin et al., 2021; Köhler et al., 2009). Even when clinical symptoms diminish, experiencing a psychosis could also have interrupted someone's role as a parent or employee, or their interpersonal relationships. This situation is reflected in our Class 5, 'insufficient well-being, sufficient recovery', in which all four sex-age of onset groups are rather equally represented. Although the degree of experienced loss might be the same for men and women, they do experience differences in the type of roles that changed, with men more often experiencing social isolation and the feeling that they cannot provide their family, whereas women more often experience disruptions in their role as caregiver (Firmin et al., 2021). Another explanation might be that the effect of having a LOP works both ways. LOP-patients might have a more (time to create a) stable life (e.g. completed education, work, family) before the onset of symptoms (Ochoa et al., 2012; Riecher-Rössler and Häfner, 2000), suggesting they are more likely to experience a better recovery process and return to well-being, but they could therefore experience a greater sense of loss as well (Malla et al., 2004). Pleading for this is our finding that men with EOP had a greater presence in Class 4, with the lowest recovery scores and sufficient well-being, but that the four sex-age of onset groups were equally represented

in Class 5, with decent recovery outcomes but the lowest well-being scores.

Lastly, all latent classes were relatively stable over time with minimal change. This is in line with a previous study finding mostly stable trajectories for societal recovery (Castelein et al., 2021; Crutzen et al., 2024), but not with all previous studies finding different trajectories of clinical and societal recovery of which the most improved over time (Chang et al., 2018; Hodgekins et al., 2015). This is likely explained by differences in study samples. Whereas in these studies (relatively young) individuals participated with a first episode of psychosis and a relatively short illness duration, the PHAMOUS-screenings included patients with a relatively long illness duration.

4.1. Strengths and limitations

Recovery from psychotic disorders is defined and operationalized in varying manners (Seeman, 2019), with some studies defining recovery purely as symptom reduction, whereas others define it as a broader concept in a more functional, societal or personal manner. It is a strength to have addressed sex and age of onset related differences in clinical as well as social and personal outcomes. In addition to the importance of addressing sex-related differences, it is also crucial to consider self-identified gender in relation to psychosis. Unfortunately, these data were not yet available in the PHAMOUS protocol at the time this study was conducted. Also, studies often use an a priori determined threshold for deciding whether someone is recovered or not. However, recovery is an individual, dynamic process which ideally should not be defined in such a (binary) way (Shinn and Carol, 2021). With the usage of LCGA, we could account for more individual variety than studies using a priori determined thresholds for recovery. This is especially important since different forms of well-being and recovery do not always co-occur.

Although the present study took a broader approach in defining well-being and recovery, the operationalization for personal recovery is suboptimal. The single-item proxy HI was previously used (e.g. Abdel-Khalek, 2006; Castelein et al., 2021), but personal recovery probably could be better measured with a broader method. However, we were restricted by the instruments included in the existing PHAMOUS-protocol of which the HI represented personal recovery best.

Even though a quite large LOP-sample was used, there were unfortunately not enough individuals with a very late onset of psychosis (61 years or older; Howard et al., 2000) to analyse results separately for this group as well.

Lastly, it is a strength to have used a sample with a relatively long illness duration, therefore representing a relatively large group of patients that is underrepresented in psychosis literature, since most papers use samples with shorter illness durations.

4.2. Implications and future research

This study showed that both sex and age of onset are important factors to consider with regard to well-being and recovery in individuals with a psychotic disorder. Also, results showed that the outcomes were relatively stable over time. For the individuals at risk for worse outcomes (i.e. men with EOP), clinicians should pay extra attention to underlying mechanisms of an insufficient well-being and recovery and on how to improve these. Moreover, although more attention is paid to sex differences in clinical recovery, e.g. dosing of antipsychotics, influence of hormones on medication (Brand et al., 2022), this does not apply to societal and personal recovery. Since current literature does not show apparent sex differences in personal recovery, considering this might not be needed, but literature regarding societal recovery is more conclusive, with women more likely to have a better societal recovery. Patients might benefit if not only literature, but also clinical guidelines and treatment protocols take these sex differences into account. Moreover, results also showed that well-being and recovery do not always co-occur. Further research could examine this interaction to find out why individuals with a better recovery not always show better well-being and how mental health care practices could

improve well-being in these individuals. Furthermore, given the fact that men and women show different distributions across diagnoses, it would be interesting to study how this is related to the different recovery and well-being outcomes. Future research also could investigate a broader range of outcomes, i.e. well-being and recovery, in the very late onset group, since this group appears to have specific needs (e.g. Kim et al., 2022).

CRediT authorship contribution statement

Linda Hoeksema: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Jojanneke Bruins:** Writing – review & editing, Visualization, Supervision, Methodology, Formal analysis, Conceptualization. **Marieke E. Timmerman:** Writing – review & editing, Supervision, Methodology, Formal analysis. **Stynke Castelein:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Informed consent

Informed consent was not obtained, but patients could opt out for the use of their data for scientific research.

Ethics approval

The study design was approved by the local ethical committee.

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Declaration of competing interest

The authors declare no competing interests.

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Appendix B. Supplementary data

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