Tecelli Domínguez-Martínez[1]
Paula Cristóbal-Narváez[2]
Thomas R. Kwapil[3]
Neus Barrantes-Vidal[2,4,5]

Clinical and Psychosocial Characterization of At-Risk Mental State and Recent Onset Psychosis Patients from an Early Psychosis Program in Barcelona (Spain)

[1] CONACYT-Dirección de Investigaciones Epidemiológicas y Psicosociales. Instituto Nacional de Psiquiatría "Ramón de la Fuente Muñiz", Ciudad de México, México
[2] Departament de Psicologia Clínica i de la Salut. Universitat Autònoma de Barcelona, Barcelona, España
[3] Department of Psychology, University of Illinois at Urbana-Champaign, USA
[4] Departament de Salut Mental. Sant Pere Claver-Fundació Sanitària. Barcelona, España
[5] Centre for Biomedical Research Network on Mental Health (CIBERSAM), Instituto de Salud Carlos III, Madrid, España

Introduction. This study aimed to describe and compare socio-demographic, background, treatment history, and service use, psychopathological and psychosocial characteristics of At-Risk Mental States (ARMS) and First-Episode Psychosis (FEP) patients from the Sant Pere Claver-Early Psychosis Program (SPC-EPP) in Barcelona.

Methods. 43 ARMS-patients and 40 FEP-patients were assessed with several clinical and psychosocial measures at study baseline.

Results. Clinical and psychosocial characteristics of the SPC-EPP sample were comparable to those of previous early psychosis studies. Overall, the socio-demographic and clinical background characteristics appeared to be mostly similar between ARMS and FEP patients. As expected, groups differed on history of previous psychiatric hospitalizations and current psychiatric treatment. The age at onset of both unspecific and prodromal symptoms, and age of first specialized psychiatric/psychological treatment were earlier in ARMS than in FEP-patients. FEP-patients showed higher scores on positive symptoms, cognitive and greater overall symptom severity than ARMS-patients. ARMS-patients showed higher scores on mania, general psychopathology and a slightly lower premorbid functioning since early-adolescence than FEP-patients.

Conclusions. Findings support the notion that ARMS-patients who seek for help can be considered as already highly dysfunctional and in need of treatment, given that they already suffer from multiple mental and functional disturbances. This supports current health care efforts in providing early access to treatment to this population and signals the need to sustain pilot early detection efforts.

Keywords: Ultra-High Risk, First-Episode of Psychosis, Early detection, Functioning, Prodrome, Schizophrenia

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Correspondence:
Neus Barrantes-Vidal
Departament de Psicologia Clínica i de la Salut
Facultat de Psicologia. Edifici B
Universitat Autònoma de Barcelona
08193 Bellaterra (Cerdanyola del Vallès), Barcelona, Spain
Tel.: 0034 93 581 38 64
Fax: 0034 93 581 21 25
E-mail: neus.barrantes@uab.cat

Características clínicas y psicosociales de pacientes con Estados Mentales de Alto Riesgo y Primeros Episodios de Psicosis de un Programa de Psicosis Incipiente en Barcelona (España)

Introducción. Este estudio tiene como objetivo describir y comparar las características sociodemográficas, clínicas y psicosociales, así como los antecedentes de tratamiento y uso de servicios, de pacientes con Estados Mentales de Alto Riesgo (EMAR) y Primeros Episodios de Psicosis (PEP) del Programa de Psicosis Incipiente-Sant Pere Claver (PPI-SPC) en Barcelona.

Metodología. 43 EMAR y 40 pacientes PEP fueron evaluados con numerosos instrumentos clínicos y psicosociales al inicio del estudio.

Resultados. Las características clínicas y psicosociales de la muestra del PPI-SPC fueron comparables con las de estudios previos de psicosis incipiente. Las características sociodemográficas, clínicas y los antecedentes fueron similares entre los grupos de pacientes. Como era de esperar, los grupos EMAR y PEP mostraron diferencias significativas en los antecedentes de tratamientos psiquiátricos previos, hospitalizaciones y tratamiento psiquiátrico actual. La edad de inicio de los síntomas inespecíficos, los síntomas prodrómicos y la edad de inicio del primer tratamiento especializado fue anterior en los pacientes EMAR que en los PEP. Los pacientes PEP mostraron mayores puntuaciones en los síntomas positivos y cognitivos, y mayor gravedad global sintomatológica

que los pacientes EMAR. Los pacientes EMAR mostraron mayores puntuaciones en manía, sintomatología general y un deterioro ligeramente mayor del funcionamiento premórbido desde la adolescencia temprana que los PEP.

Conclusiones. Los resultados apoyan la noción de que los pacientes EMAR que buscan atención pueden considerarse como una población con un deterioro psicosocial importante y con necesidad de tratamiento, ya que padecen de múltiples alteraciones mentales y funcionales. Estos resultados respaldan la conveniencia de los esfuerzos actuales de detección e intervención temprana en esta población.

Palabras clave: Alto Riesgo, Primer episodio de psicosis, Detección temprana, Funcionamiento, Pródromo, Esquizofrenia

INTRODUCTION

In schizophrenia and other psychotic disorders there is usually a "prodomal" or "pre-psychotic" phase of the disorder in which a change from premorbid functioning occurs[1]. Essentially, these terms refer to a period of pre-psychotic disturbance, representing a deviation from a person's previous experience and behavior, usually defined as the period occurring from the emergence of the first noticeable symptoms to the appearance of the first prominent psychotic symptoms. It may be lengthy, lasting on average between 1 and 5 years[2], and is often associated with substantial levels of psychosocial impairment and disability[3].

Clinical research findings in recent decades suggest that the benefits of implementing treatment as early as possible in the course of psychotic disorders may at least help to improve the course of the disorder and reduce its long-term impact[4]. Moreover, investigating and evaluating patients at the early stages of psychosis, either prior to the onset of frank psychotic symptoms or at their First-Episode of Psychosis (FEP), limits the potential confounding effects of illness severity, progression, or long-term exposure to antipsychotic drugs.

The possibility to monitor prospectively individuals at heightened risk for developing psychosis lies in the recent identification of a population that demonstrates a prodromal or clinical high-risk factors for subsequent psychosis, established as "At-Risk Mental State" (ARMS), implying that a subthreshold syndrome can be regarded as a risk factor for subsequent psychosis, but that psychosis is not inevitable[5]. However, although several studies have indicated that the ARMS-criteria are valid and reliable for predicting psychosis[6], their implications for early diagnosis and treatment runs into problems due to the wide variability between individuals and the lack of specificity of many of their features[7]. Moreover, despite the establishment of multiple successful clinical and research programs focused on early detection and intervention in psychosis, there is a lack of consensus and operational definition for what is commonly referred to as FEP, since it is typically used to refer to individuals early in the course of a psychotic disorder or treatment rather than individuals who are truly in the midst of a first 'episode' of disorder. Operational definitions for FEP fall largely into three categories: i) first treatment contact, ii) duration of antipsychotic medication use, and iii) duration of psychosis[8].

Given the complex etiology and heterogeneous clinical manifestation of psychosis, an important goal of research is to better characterize the early phases of psychosis with the purpose of improving early detection and reaching a valid cross-cultural definition of the high-risk and FEP populations. Furthermore, considering that both help seeking and pathways to care depend on various factors such as gender, cultural and economic background, and the structure and accessibility of local mental health care systems[9], another goal of research is to describe the particular socio-demographic and clinical background features of the early psychosis population from different treatment programs who belong to specific cultural and socio-economic contexts, in order to better understand the different problems related to the delay in the help seeking across several countries and, thus, find better ways to deliver treatment as early as possible at the onset of the disorder. In this sense, this study aims at examining socio-demographic, clinical background, treatment history, current service use, psychopathological and psychosocial characteristics of ARMS and FEP patients who are being treated in the Sant Pere-Claver Early Psychosis Program (SPC-EPP) in Barcelona (Spain)[10]. Additionally, these two groups are compared in order to characterize commonalities and differences between the at-risk and onset of disorder stages, with the aim of increasing our knowledge of the ARMS population as defined by current ARMS-criteria.

METHODS

The present study is part of a larger longitudinal study currently being carried out in the SPC-EPP[10]. The project was approved by the local ethic committee and it conforms to the provisions of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Patients' inclusion criteria were age between 14 and 40 years old, IQ ≥ 75, and a proper command of Spanish language. ARMS-criteria was established by the Comprehensive Assessment of At-Risk Mental States (CAARMS)[11] and/or the Schizophrenia Proneness Instrument-Adult version (SPI-A)[12].

FEP-patients met DSM-IV-TR[13] criteria for any psychotic disorder or affective disorder with psychotic symptoms as established by the Structured Clinical Interview for DSM-IV(SCID-I)[14].

The onset of prodrome was defined as the earliest clinically significant deviation from the patient's premorbid personality[15] and was established considering the first appearance of either attenuated positive or negative symptoms[16]. Duration of Untreated Illness (DUI) was defined as the time interval since the onset of prodromal symptoms to receiving the first specialized psychiatric and/or psychological treatment[17], whereas Duration of Untreated Psychosis (DUP) was defined as the time interval between the onset of psychotic symptoms and treatment initiation[18]. All available information provided by patients, family and clinical history was used to set DUI, DUP and the age at onset of unspecific, prodromal and psychotic symptoms.

Categorical diagnosis was establish by means of SCID-I[14]. Prodromal symptoms of ARMS-patients were assessed with the CAARMS[11]. Psychopathology of all patients was assessed with the Positive and Negative Syndrome Scale (PANSS)[19]; the Calgary Depression Scale (CDS)[20]; the Young Mania Rating Scale (YMRS)[21]; and the Clinical Global Impression scale (CGI)[22]. Quantitative ratings of personality dysfunction was assessed with the Cluster A Module of the Structured Interview of Personality Disorders (SCID-II)[23]. Substance Abuse and Dependence DSM-IV criteria were established by the SCID-I[11]. The SPI-A[12], a semi-structured interview for assessing basic symptoms, was administered to both ARMS and FEP patients to establish the Cognitive-Perceptive Disturbances (COPER) and Cognitive Disturbances (COGDIS) risk criteria.

The Social and Occupational Functioning Assessment Schedule (SOFAS)[24] and the Global Functioning: Social and Role Scales (GF-Social and GF-Role)[25] were used to assessed functional impairment. Premorbid functioning was assessed by the Premorbid Adjustment Scale (PAS),[26] and quality of life was assessed by the World Health Organization Questionnaire of Quality of Life-Brief Version (WHOQOL-BREF)[27].

RESULTS

Intake Diagnosis and Socio-demographic Characteristics

The sample was comprised of 43 ARMS and 40 FEP patients. As shown in Table 1, almost all ARMS-patients met criteria for the Attenuated Psychosis Symptoms (APS) group (90%) and 21% belonged to more than one high-risk group criteria according to CAARMS[11]. Over half of the 36 ARMS-patients assessed with the SPI-A, met at least one of the COPER/COGDIS criteria and almost all of them met both APS and either COPER or COGDIS criteria. Almost half of FEP-patients met criteria for Psychotic Disorder Not Otherwise Specified. From 25 FEP-patients assessed with SPI-A, around half met one of the COPER or COGDIS criteria and 40% meet both COPER/COGDIS-criteria.

The socio-demographic details of the sample are shown in Table 2. Chi-square or Fisher's exact test were used to compare categorical variables, while Student t-test was used to compare dimensional variables. Significant differences were found on age and current occupation. The ARMS-group was younger than the FEP-group and almost half of them were studying, while over half of the FEP-patients were unoccupied/unemployed. Differences on age could explain that only a few ARMS-patients completed college studies (9%) and almost all of them were lived with the family of origin, unlike those of the FEP-group. However, these differences were not statistically significant. Groups did not differ in terms of gender, immigrant status, ethnicity, education, marital status or living situation.

Clinical Background, Treatment History and Current Service Use

No differences between groups were found on history of previous treatments, suicide attempts, lifetime abuse or dependence of alcohol, cannabis or other substances. As to be expected, significant differences between groups were found on previous psychiatric hospitalization (Fisher's Exact Test p=0.000), given that most FEP, but not ARMS-patients, were previously hospitalized. Regarding family psychiatric history, the most frequent disorders present in relatives of both groups were psychotic and affective disorders. Groups did not differ on this variable.

Information about history of current disorder, current treatment and use of service at SPC-EPP is detailed in Table 3. ARMS-patients showed an earlier age at onset of both unspecific and prodromal symptoms, as well as an earlier age of first specialized psychiatric/psychological treatment than the FEP-group. Age at onset of psychotic symptoms in FEP-patients was around 24 years old. No differences were found between groups on DUI. The origin of the psychiatric/psychological demand did not differ between groups. The current main reason for consulting a mental health service in the ARMS-group was mood problems, whereas in the FEP-group was positive psychotic symptoms. As to be expected, significant differences were found on current use of drugs, as FEP-patients were taking more antipsychotic and anticholinergic medications than ARMS-patients, whereas ARMS-patients were taking more antidepressants than FEP-patients.

Table 1 ARMS and FEP patients' diagnostic intake criteria

	ARMS N=43		FEP N=40	
	n	%	n	%
ARMS Intake criteria (CAARMS)				
APS	39	90.3	NA	
BLIPS	3	7.1	NA	
TSRF	9	20.9	NA	
APS + BLIPS	2	4.8	NA	
APS + TSRF	5	11.9	NA	
BLIPS + TSRF	2	4.8	NA	
Intake COPER/COGDIS criteria (SPI-A)[a]	**N=36**		**N=25**	
COPER	28	77.8	14	56.0
COGDIS	25	69.4	12	48.0
COPER+COGDIS	22	61.1	10	40.0
ARMS Intake criteria (CAARMS+SPI-A)[a]	**N=28**			
COPER + APS	27	96.4	NA	
COPER + BLIPS	3	11.1	NA	
COPER + TSRF	5	17.9	NA	
	N=25			
COGDIS + APS	24	96.0	NA	
COGDIS + BLIPS	2	8.3	NA	
COGDIS + TSRF	3	12.0	NA	
	N=22			
COPER + COGDIS + APS	21	95.5	NA	
COPER + COGDIS + BLIPS	2	9.5	NA	
COPER + COGDIS + TSRF	3	13..6	NA	
FEP Intake criteria (DSM-IV diagnoses)			**N=40**	
Schizophrenia	NA		7	17.5
Schizophreniform disorder	NA		3	7.5
Brief psychotic disorder	NA		3	7.5
Psychotic disorder NOS	NA		18	45.0
Bipolar disorder I	NA		8	20.0
Bipolar disorder NOS	NA		1	2.5

ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; APS: Attenuated Psychotic Symptoms; BLIPS: Brief Limited Intermittent Psychotic Symptoms; TSRF: Trait and State Risk Factors; SPI-A: Schizophrenia Proneness Instrument for Adults; COPER: Cognitive-Perceptive Disturbances; COGDIS: Cognitive Disturbances; CAARMS: Comprehensive Assessment of At-Risk Mental States; DSM-IV: Diagnostic Statistic Manual; SCID-I: Structured Clinical Interview Axis I Disorders; SD: Standard Deviation; NA: Not applicable; NOS: Not Otherwise Specified; NA: Not Applicable.
[a]Given that the Spanish adaptation of the SPI-A was not available at the beginning of the study, not all patients completed this assessment

Clinical and Psychosocial Characteristics

As shown in Table 4, differences between groups were found on mania (YMRS) and general psychopathology (as measured by the PANSS), in which the ARMS-group showed higher scores than the FEP-group. Moreover, FEP-patients showed higher severity ratings than ARMS-patients on positive and cognitive symptoms, and in overall severity as assessed by CGI. No differences between groups were found on depression, negative symptoms or personality disorder scores.

Description and comparisons of premorbid adjustment, current functioning and quality of life are presented in Table

Table 2 Sociodemographic characteristics of the sample

	ARMS N=43		FEP N=40		Statistics
	n	%	n	%	
Age (M±SD)	20.6±4.0		26.0±5.8		t (68)=-4.8***
Range of age	14-30		16-40		
Gender					Fisher=0.82
Males	28	65.1	25	62.5	
Females	15	34.9	15	37.5	
Immigrant					Fisher=0.32
No	34	79.1	27	67.5	
Yes	9	20.9	13	32.5	
Ethnicity					Fisher=0.81
Caucasian-white	30	69.8	29	72.5	
Other[a]	13	30.2	11	27.5	
Education					Fisher=0.07
Secondary education	39	90.7	30	75.0	
College studies	4	9.3	10	25.0	
Occupation					χ^2=9.0**; *df*=2
Unemployed/Unoccupied	12	27.9	23	57.5	
Worker/Employee	12	27.9	10	25.0	
Student	19	44.2	7	17.5	
Marital Status					Fisher=0.08
Married/Cohabiting/Going out with someone	4	9.3	10	25.0	
Single/Separated/Divorced	39	90.7	30	75.0	
Living Situation[b]					
Alone	1	2.3	1	2.5	
With the family of origin	42	97.7	28	70.0	
With partner	0	0	6	15.0	
With friends/Roommate	0	0	5	12.5	

ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation.
[a]Other ethnicity includes Asian, Arab, Latin-American, Eastern European and Mixed.
[b]The chi-square is uninterpretable because minimum expected value is < 5.
**p<0.01
***p<0.001

5. PAS-scores in both groups indicate a slight and gradual decline of premorbid functioning from early-adolescence. Significant differences between groups were found on premorbid functioning during early-adolescence, late-adolescence and adulthood, in which ARMS-patients showed a worse performance than FEP-patients since early-adolescence. Current level of functioning, as reflected in all functional measures was considerably low and similar in both groups, indicating a functional impairment ranging from moderate to severe. Quality of life also appeared as already compromised in both groups, and did not differ between them.

CONCLUSIONS

The current study describes and compares the socio-demographic, clinical background, treatment history, psychopathological and psychosocial characteristics of ARMS and FEP patients treated in the SPC-EPP. Findings indicate scarce differences between ARMS and FEP groups on clinical and psychosocial features, which supports current health care efforts in providing early access to treatment to individuals at clinical high-risk of psychosis, as well as the need to sustain early detection efforts.

Table 3 Treatment history and current service use

	ARMS N=43		FEP N=40		Statistics
	Mean±SD		Mean±SD		
History of Current Disorder					
Age at onset of unspecific symptoms	14.5±4.1		21.6±7.0		t (61)=-5.4***; *d*=-1.23
Age at onset of prodromal symptoms	17.4±3.4		23.1±6.0		t (61.8)=-5.2***; *d*=-1.2
Age at onset of psychotic symptoms	NA		24.1±6.2		
Age at first specialized psychiatric/psychological visit	18.4±4.5		24.1±6.4		t (70)=-4.7***; *d*=-1.0
Duration of Untreated Illness (DUI) (weeks)	94.1±185.4		72.1±144.9		t (81)=0.60; *d*=0.13
Duration of Untreated Psychosis (DUP) (weeks)	NA		55.1±100.2		
	n	%	n	%	
Origin of Current Psychiatric/Psychological Demand					χ^2=1.9; *df*=2
Patient	18	41.8	16	40.0	
Family	14	32.5	18	45.0	
Medical service/Community services/judicial service	11	25.6	6	15.0	
Current Main Reason for Consulting a Mental Health Service					
Thought problems/suspiciousness or delusions	5	11.6	14	35.0	
Sensory perception alterations/hallucinations	5	11.6	9	22.5	
Relationships/socialization/isolation problems	3	7.0	4	10.0	
Behavioral problems/aggressiveness	1	2.3	4	10.0	
Mood condition/depression/sadness/low self-esteem	12	27.9	4	10.0	
Anxiety/panic attacks	4	9.3	1	2.5	
Poor academic/work performance	6	14.0	1	2.5	
Other reason (sleep problems/somatic complaints/ substances/ stress/cognitive alterations/obsessions)	7	16.2	3	7.5	
Current PsychiatricTreatment					
Antipsychotic medication	15	34.9	40	100	Fisher=0.00***
Anxiolytic medication	20	46.5	26	65.0	Fisher=0.12
Antidepressant medication	28	65.1	9	22.5	Fisher=0.00***
Mood stabilizer medication	0	9	2	5.0	Fisher=0.22
Anticholinergic medication	0	9	11	27.5	Fisher=0.00***
Anticonvulsant medication	1	2.3	1	2.5	Fisher=1.0
Current Psychological Treatment					
None	0	0	2	5.0	Fisher=0.02
Yes	43	100	38	95.0	
Individual Psychotherapy	26	60.5	23	57.5	Fisher=0.38
Group Psychotherapy	24	55.8	21	52.5	Fisher=0.66
Family psychotherapy	10	23.3	14	35.0	Fisher=0.28
Assertive Community Treatment-Case Management	1	2.3	1	2.5	Fisher=1.0
Private psychotherapy	2	4.7	2	5.0	Fisher=1.0

ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation.
***p< 0.001

Table 4 Descriptive data and comparison of ARMS and FEP groups on clinical measures

	Possible range	ARMS N=43		FEP N=40		Mean Comparison t-test
		Range	Mean±SD	Range	Mean±SD	
Prodromal symptoms (CAARMS)						
Positive symptoms-S	0-24	0-18	9.5±3.6	NA	NA	NA
Positive symptoms-F	0-24	0-21	10.4±4.0	NA	NA	NA
Cognitive change-S	0-12	2-10	4.3±1.8	NA	NA	NA
Cognitive change-F	0-12	1-6	3.4 ±1.4	NA	NA	NA
Emotional disturbance-S	0-18	0-13	5.1±2.9	NA	NA	NA
Emotional disturbance-F	0-18	0-18	6.7±4.3	NA	NA	NA
Negative symptoms- S	0-18	3-16	7.8±3.0	NA	NA	NA
Negative symptoms-F	0-18	3-18	9.1±3.0	NA	NA	NA
Behavioural change-S	0-24	3-16	8.6±3.4	NA	NA	NA
Behavioural change-F	0-24	3-17	8.5±3.8	NA	NA	NA
Motor/physical changes-S	0-24	0-12	4.7±3.23	NA	NA	NA
Motor/physical changes-F	0-24	0-11	4.2±3.4	NA	NA	NA
General psychopathology-S	0-48	2-26	13.7±5.8	NA	NA	NA
General psychopathology-F	0-48	1-34	12.9±6.3	NA	NA	NA
Affective Symptoms						
Mania (YMRS)	0-60	0-24	4.8±4.8	0-20	2.6±3.8	2.2*; *d*=0.51
Depression (CDS)	0-27	0-17	6.7 ±4.9	0-18	5.2±4.8	1.3; *d*=0.31
Symptom severity						
PANSS-Positive	7-49	7-22	13.0±3.2	7-24	13.4±4.1	-0.5; *d*=-0.11
PANSS-Negative	7-49	8-34	19.1±5.8	7-31	17.6±6.6	1.1; *d*=0.24
PANSS-General	16-112	19-66	36.8±9.0	17-52	31.5±8.2	2.7**; *d*=0.62
CGI-Positive	1-7	1-4	2.0±0.9	1-6	2.5±1.3	-2.0*; *d*=-0.45
CGI-Negative	1-7	1-5	3.0±1.1	1-5	3.5±1.1	-1.7; *d*=-0.45
CGI-Depressive	1-7	1-5	3.0±1.2	1-5	2.9±1.3	0.30; *d*=0.08
CGI-Cognitive	1-7	1-5	2.2±1.1	1-5	2.9±1.2	-2.3*; *d*=-0.61
CGI-Overall	1-7	1-5	2.9±0.8	1-5	3.4±1.0	-2.6*; *d*=-0.55
Personality Disorders (SCID-II)						
Schizotypic Personality Disorder	9-27	9-23	14.1±2.9	9-21	13.3±3.4	0.94; *d*=0.25
Schizoid Personality Disorder	7-21	7-18	10.2±3.1	7-19	9.2±2.5	1.4; *d*=0.36
Paranoid Personality Disorder	7-21	7-18	10.3±3.3	7-18	10.3±3.8	0.21; *d*=0

ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation; CAARMS: Comprehensive Assessment of At-Risk Mental States; S: Severity; F: Frequency; YMRS: Young Mania Rating Scale; CDS: Calgary Depression Scale; PANSS: Positive and Negative Syndrome Scale; CGI: Clinical Global Impression; SCID-II: Structured Clinical Interview-Axis II; NA: Not applicable; d: Cohens d'.
*p<0.05; **p<0.01

Table 5 Descriptive data and comparison between ARMS and FEP groups on psychosocial measures

	Possible range	ARMS N=43		FEP N=40		Mean Comparison t-test
		Range	Mean±SD	Range	Mean±SD	
Premorbid adjustment (PAS)[a]						
			N=43		N=40	
Childhood	0-1	0-0.54	0.31±0.14	0-0.63	0.25±0.15	1.8; *d*=0.41
			N=43		N=40	
Early adolescence	0-1	0.10-0.87	0.41±0.16	0-0.90	0.30±0.18	2.6*; *d*=0.65
			N=38[d]		N=36[d]	
Late adolescence	0-1	0.20-0.90	0.44±0.17	0-67	0.33±0.17	2.7**; *d*=0.65
			N=30[e]		N=32[e]	
Adulthood	0-1	0.28-0.83	0.49±0.15	0.09-0.78	0.41±0.19	3.3**; *d*=0.47
Current Social Functioning[b]			N=43		N=40	
SOFAS	0-100	25-80	57.3±10.3	40-80	59.7±10.1	-1.1; *d*=-0.24
GF-Social	0-10	2-8	5.9±1.3	3-8	6.3±1.3	-1.6; *d*=-0.31
GF-Role	0-10	3-8	5.8±1.2	4-8	5.6±1.3	0.61; *d*=0.16
Quality of Life (WHOQoL-BREF)[c]			N=41		N=25[f]	
Physical health	4-20	4.6-18.9	13.4±3.1	8.6-18.3	14.2±2.7	-1.1; *d*=-0.28
Psychological health	4-20	4.7-18.7	11.9±3.6	5.3-18.0	12.8±3.0	-1.2; *d*=-0.27
Social relationship	4-20	4.0-17.3	11.7±3.7	6.7-18.7	12.5±3.2	-0.83; *d*=-0.23
Environment	4-20	7.5-18.0	13.4±2.9	10.0-17.5	14.0±2.1	-0.87; *d*=-0.24
Overall QoL	2-10	2.0-10.0	5.9±1.9	4.0-10.0	6.6±1.4	-1.5; *d*=-0.42

ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation; PAS: Premorbid Adjustment Scale; SOFAS: Social and Occupational Functional Assessment Scale; GF-Social: Global Functioning-Social scale; GF-Role: Global Functioning-Role scale; WHOQOL-BREF: World Health Organization for Quality of Life-Bref.
[a]Lower scores indicate the "healthiest" level of functioning.
[b]Higher scores indicate greater levels of functioning.
[c]Higher scores denote higher quality of life.
[d]Late Adolescence subscale of PAS was not applicable for patients younger than 15 years old.
[e]Adult subscale of PAS was not applicable for patients younger than 18 years old.
[f]Data from WHOQOL-BREF were available only for 25 FEP patients because it was not initially included in the protocol assessment of FEP patients, but it was included later.
*p<0.05; **p<0.01

Consistent with recent findings, ARMS-patients were younger and were mostly studying or working unlike those with FEP[9]. Overall, the socio-demographic and clinical background characteristics appeared to be mostly similar between ARMS and FEP patients, including gender, immigrant status, ethnicity, previous psychiatric/psychological treatments, history of suicide attempts, substance abuse/dependence, family history of psychiatric disorders, and origin of current psychiatric/psychological demand. Several similarities on the clinical antecedents between ARMS and FEP patients were also reported by Zimbrón et al.[28]. However, given that many socio-demographic and clinical background characteristics vary depending on socio-economic contexts and demographic profiles, other comparative studies carried out in different locations would be of interest.

It is noteworthy that more than half of ARMS-patients (65.1%) take antidepressant medication. This picture is consistent with the predominant feature of affective dysfunction characterizing this population, and with evidence indicating that the use of antidepressants might have similar efficacy in preventive efforts as low doses of antipsychotics due to their neuroprotective effect[29]. Also, they have a less adverse profile of side effects and associated morbidity, which may help in increasing treatment adherence in such vulnerable population.

The earlier age at onset of both unspecific and prodromal symptoms in ARMS possibly reflects a long course of symptoms since early-adolescence, which might also explain why the age at onset of receiving the first specialized psychiatric/psychological treatment was earlier in ARMS than in FEP. Interestingly, ARMS sought professional help during the prodromal phase (current moment), whereas FEP did not receive their first specialized treatment until the onset of psychotic symptoms. This is consistent with the proportion of FEP (around 57.5%) whose main reason for seeking mental health help was the presence of psychotic symptoms (delusions/hallucinations), whereas for ARMS was the presence of unspecific and/or prodromal symptoms such as depressed mood, sleep problems, poor academic/work performance, sensory perception anomalies and suspiciousness. It is important to note that many ARMS could be detected and treated during the prodrome, probably as a result of the improvement and effectiveness of early detection efforts in the primary health care.

The mean of DUI in our sample was within the average of 22 and 166.4 weeks reported by several studies[30,31]. Furthermore, according with most previous studies, the mean DUP in our FEP-sample was within a mean of around 1-2 years[2,32] although it was longer than that reported by both the EPPIC large long-term follow-up study of FEP in Australia[12] and the Prevention Program for Psychosis (P3) of Oviedo (Spain)[33]. This might be explained for the still short live of the SPC-EPP as compared with other sites.

The comparison of the clinical and psychosocial characteristics of SPC-EPP with those of other sites is not entirely easy, given the notable differences in measurement between research programs worldwide. Overall, though, the socio-demographic, clinical and functional features of the SPC-EPP sample were mostly comparable to those of previous studies. Consistent with the literature, ARMS-patients showed prominent negative and anxiety symptoms, as well as marked functional impairment[5,28,34-36]. In accordance with previous findings, APS was by far the most common inclusion criterion met by ARMS-patients[37-40]. Regarding the SPI-A high-risk criteria, most of ARMS-patients met the COPER-criteria (77.8%), followed by the COGDIS-criteria (69.4%) and over the half meeting both COPER/COGDIS-criteria. Considering that the COPER/COGDIS-criteria show an overlap of about 50% in their respective defining symptoms, our findings are comparable with previous studies in which most of the subjects meeting COGDIS also met the COPER-criteria[12]. Moreover, severity and frequency of prodromal positive symptoms scores (assessed by the CAARMS), as well as global functioning impairment scores (assessed by the SOFAS and GF-scales) of our ARMS-patients were comparable to those reported by most of ARMS studies[25,31,38,41-44]. The FEP-sample showed some differences from previous studies, possibly due to the high heterogeneity of FEP definitions and, thus, sample characteristics across studies[15]. For example, SOFAS scores were higher in our FEP-sample compared to those of the EPPIC study[15] and the OPUS Danish trial sample[45], which indicates a greater level of functioning of our FEP-sample. It is attractive to speculate that the intensity of family interventions conducted at the SPC-EPP[10] along with the prototypical family support in patient's daily living activities and warmth characterizing Latino and Mediterranean families (unlike those of Anglo cultures that emphasize more values such as autonomy and independence)[46] may have an effect on the functional improvement of our FEP-group[47,48].

Overall, findings show scarce psychopathological and functional differences between ARMS and FEP groups. However, ARMS-patients showed higher severity than those of FEP on mania (probably because they presented higher scores on irritability, sleep and thought disorder problems), as well as on general psychopathology, which is consistent with the frequent presence of mood or/and anxiety disorder comorbidity on the majority of ARMS[49]. FEP-patients showed higher severity ratings than ARMS on positive and cognitive symptoms and on overall severity as assessed by CGI, which indicates that, as to be expected, these patients presented greater severity on those symptoms that characterize the chronic course of schizophrenia. It is noteworthy that groups did not differ on positive or negative PANSS ratings, which could be explained by differences on antipsychotic medication, so maybe FEP-patients were more stabilized than ARMS at the moment of the assessment.

The comparison of premorbid functioning between groups of individuals with early psychosis has been little explored. Addington et al.[50] did not find differences in terms of premorbid functioning between ARMS and FEP or multi-episode schizophrenia patients. However, in our sample, groups differed on premorbid functioning during the early and late adolescence and adulthood, with ARMS showing a slightly worse performance than the FEP-group. These findings are consistent with the fact that the onset of both unspecific and prodromal symptoms of ARMS was around early-adolescence (unlike FEP-patients, in whom illness onset was at early-adulthood), probably influencing their development of interpersonal relationships and school

performance. Thus, the difficulties in these areas of psychosocial development since early-adolescence could be reflected in the later worse functional outcome of ARMS at late-adolescence and adulthood[51], and may in fact have encouraged help seeking[50]. These findings support the notion that besides being a population at-risk, ARMS-patients have to be considered as already highly dysfunctional and in need for treatment, not only because they suffer from multiple mental and functional disturbances, but because they were seeking help[36]. This issue borders on the recent inclusion of an attenuated psychosis syndrome into the DSM-5[52]. Although this should facilitate early detection and intervention efforts, further research and reliable assessment in clinical practice should improve their diagnostic validity[53]. Considering that the predominant ARMS approach based on the presence of positive symptoms (with subthreshold severity and/or frequency) is still under review, it would be important to consider the COPER/COGDIS symptoms[12] as a complementary risk criterion that broadens the spectrum of ARMS-criteria in order to improve the detection of the 'early-psychosis prodrome' instead of the 'late prodrome', as it has been suggested by the EPOS study[36]. Furthermore, it becomes crucial to take into account specific combinations of academic, social and cognitive impairments, as well as disorganization/odd behavior[54], given that the decline in psychosocial functioning has repeatedly been demonstrated to be an important feature of at-risk samples and it has shown to be a predictor of conversion to psychosis[34,55-57].

Consistent with several studies, our findings demonstrate significant decline in psychosocial functioning in the early-stages of the psychosis continuum[28,35,51,58]. Therefore, it is important to improve early detection, reduce DUP/DUI and offer adequate treatment as soon as symptoms cause significant distress, but, specially, before functional impairments develop.

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