



## Anhedonia and suicidal ideation in young people with early psychosis: Further findings from the 2-year follow-up of the ReARMS program

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### ABSTRACT

Hedonic deficits have been extensively studied in schizophrenia, but little is known about their association with suicidal ideation in early psychosis. The aim of this research was to examine the relationship between anhedonia and suicidal thoughts across a 2-year follow-up period in people with First Episode Psychosis (FEP) and at Ultra High Risk (UHR) of psychosis. Ninety-six UHR and 146 FEP, aged 13–35 years, completed the Comprehensive Assessment of At-Risk Mental States (CAARMS) and the Beck Depression Inventory-II (BDI-II). The BDI-II “Anhedonia” subscale score to assess anhedonia and the CAARMS “Depression” item 7.2 subscore to measure depression were used across the 2 years of follow-up. Hierarchical regression analyses were performed. No difference in anhedonia scores between FEP and UHR individuals was found. In the FEP group, a significant enduring association between anhedonia and suicidal ideation was found at baseline and across the follow-up, independent of clinical depression. In the UHR subgroup, the enduring relationship between anhedonia and suicidal thoughts were not completely independent from depression severity. Anhedonia is relevant in predicting suicidal ideation in early psychosis. Specific pharmacological and/or psychosocial interventions on anhedonia within specialized EIP program could reduce suicide risk overtime.

### 1. Introduction

Anhedonia is the inability to feel pleasure in situations or activities that are normally pleasing (Pelizza et al., 2012). Recent meta-analysis revealed a robust association between anhedonia and current suicidal ideation, independent of clinical depression severity and psychiatric disorders (Ducasse et al., 2018). Traditionally, *anhedonia* has been considered as a key symptom of both schizophrenia and major depression, as well as a marker of psychosis vulnerability within the schizotypy construct (Naguy et al., 2020). Along the clinical staging of psychosis, also Ultra-High Risk (UHR) individuals are characterized by hedonic deficits (Jhung et al., 2016), which are currently considered as putative predictors of both psychosis conversion (Bang et al., 2019) and poor

social/role functioning (Cohen et al., 2020). However, there is some evidence that anhedonia is different in psychosis and in major depressive disorder (Strauss and Gold, 2012). Specifically, schizophrenia spectrum disorders seem to be characterized by a disorganization (rather than a deficiency) in reward processing and cognitive function, including energy expenditure and focus on irrelevant cues (Kring and Barch, 2014; Gooding and Pflum, 2014; Lambert et al., 2018). Differently, major depressive disorder has been characterized by deficits in anticipatory pleasure, development of reward associations, and integration of information from past experience (Pelizza and Ferrari, 2009; Pelizza et al., 2021a; Pizzagalli and Der-Avakian, 2022).

In a recent 2-year longitudinal study, we examined the risk of suicide in a clinical sample of UHR adolescents and young adults within an

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“Early Intervention in Psychosis” (EIP) program (Pelizza et al., 2020a). Our findings specifically showed a significant association between *suicidal ideation* (rated by the “Suicidal thoughts and wishes” item 9 of the Beck Depression Inventory – II Edition [BDI-II]) (Beck et al., 2006) and “Anhedonia” (as measured on item 4.3 subscore of the Comprehensive Assessment of At-Risk Mental States [CAARMS]) (Yung et al., 2005). To the best of our knowledge, this was the first longitudinal study investigating the relationship between anhedonia and suicidal ideation in UHR subjects.

However, our follow-up study had some methodological limitations and additional data analyses could further be done, especially to better explore the association between suicide risk and hedonic deficit. First, CAARMS “Anhedonia” is just a single item and its subscores may be quite unstable overtime. Thus, more stable scores computed as a sum of different items (such as the BDI-II “Anhedonia” subscale score, combining items 4, 12, 15 and 21 subscores) (Winer et al., 2014a) should be preferred. Second, given the high prevalence of depressive disorders in UHR individuals at the first contact with adolescent and adult mental health services (Pelizza et al., 2018), the potential influence of depression on the relationship between suicidal ideation and anhedonia should also be controlled. Specifically, as suicidal thoughts was rated after both 12- and 24-month follow-up periods in our previous longitudinal analysis, whether anhedonia symptoms predicts suicidal ideation both at baseline and after the 2 years of follow-up could also be examined. Third, in our previous study, we did not compare these relationships between UHR individuals and help-seeking peers with First Episode Psychosis (FEP).

As evidence showed that recent change in anhedonia severity was most predictive of suicidal ideation (Hawes et al., 2018), the main aim of the present retrospective research was thus to investigate the association between current (2-week) anhedonia levels and current (2-week) suicidal thoughts along a 2-year follow-up period in distinct clinical samples of adolescents and young adults identified through the CAARMS criteria (i.e., FEP vs. UHR vs. non-UHR/FEP) (Yung et al., 2005).

## 2. Methods

### 2.1. Setting and subjects

All the participants were enrolled within the “Reggio Emilia At-Risk Mental States” (ReARMS) program between September 2012 and March 2019 (for details on the ReARMS protocol, see Pelizza et al., 2020b).

**Inclusion criteria** were: (a) age 13–35 years; (b) specialist help-seeking request; and (c) UHR status (i.e. Brief Limited Intermittent Psychotic Symptoms [BLIPS], Attenuated Psychotic Symptoms [APS] or Genetic Risk and Functioning Deterioration [GRFD] syndrome) or FEP diagnosis (with a Duration of Untreated Psychosis [DUP] <2 years) at baseline, in accordance with the CAARMS UHR/FEP criteria (Yung et al., 2005). A DUP (defined as the time period [in weeks] between the onset of overt psychotic symptoms and the first administration of antipsychotic therapy) (Ran et al., 2018) of <2 years was selected because it is usually considered the limit to start a specialized care protocol within the “Early Intervention in Psychosis” paradigm (Leuci et al., 2020).

**Exclusion criteria** were: (a) previous history of non-affective and affective psychosis (in accordance with the DSM-IV-TR criteria) (APA, 2000); (b) past exposure to antipsychotics or antipsychotic intake for no more than 2 months in the current illness episode; (c) current substance dependence (according to the DSM-IV-TR criteria); (d) known intellectual disability (i.e. Intelligence Quotient <70); and (e) neurological disorders or other medical condition associated with psychiatric symptoms. In accordance to the CAARMS psychosis criteria, we considered past exposure to antipsychotics (i.e. in previous illness episodes, before the ReARMS enrollment) as an equivalent of a past psychotic episode. Indeed, the CAARMS FEP threshold was specifically defined as that at which antipsychotics would probably be started in the common clinical practice (Raballo et al., 2020).

All subjects enrolled within the ReARMS protocol and their parents (if minors) agreed to participate to the research and gave their informed consent prior to their inclusion in this study. Local ethical approval was obtained (AVEN Ethics Committee protocol no. 0066667/2019). The present study has been also carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments including humans. The data that support the findings of this research are available on request from the authors. The data are not publicly available due to privacy and/or ethical restrictions.

### 2.2. Measures

The psychopathological assessment for this research included the CAARMS and the BDI-II. The CAARMS is a clinical interview specifically designed to cover different aspects of attenuated psychopathology and to identify UHR and FEP individuals. In the current research, we used the approved Italian version of the CAARMS (CAARMS-ITA) (Raballo et al., 2013), which showed good psychometric properties in Italian clinical samples of patients with early psychosis (Pelizza et al., 2020c). Specifically, the CAARMS-ITA had an excellent interrater reliability (Paterlini et al., 2019). The Cohen’s kappa for CAARMS diagnoses was 0.845 ( $p < 0.001$ ), and the Intra-Class Correlation coefficients of the total score and the seven CAARMS subscale scores ranged from 0.965 to 1.000. For the specific purpose of this research, we used the CAARMS “Depression” item 7.2 to rate the severity of clinical depression. Specifically, it is a 7-point component (i.e. from 0 = “absent” to 7 = “very severe”) that covers depressive mood, hopelessness, motivation in usual activities, appetite, sleep continuity and future openness over a 12-month period, so capturing longitudinal changes in the clinical status (Yung et al., 2005).

The BDI-II is a 21-item self-report instrument to measure recent (2-week) depression severity in individuals aged 13–80 years. Its items are rated following a 4-point Likert scale (i.e. from 0 = “absent” to 3 = “very severe”) and are usually summed in a single total score. According to Winer et al. (2014a), recent change of anhedonia levels was rated using the BDI-II “Anhedonia” subscale, summing BDI-II items 4 (“Loss of Pleasure”), 12 (“Loss of Interest”), 15 (“Loss of Energy”) and 21 (“Loss of Interest in Sex”) item subscores. In the current research, we used the approved Italian adaptation of the BDI-II, which showed good psychometric properties in Italian clinical samples (Sica et al., 2007). Specifically, in the present study, Intra-Class Correlation (ICC) coefficients of >0.75 for all BDI scores were found, suggesting a good short-term (2-week) test-retest reliability. As for internal consistency, Cronbach’s alpha coefficients of >0.80 for BDI-II total and subscale scores were also observed. In order to avoid a psychometric overlapping among measures on anhedonia and depression severity in our statistical analysis, we preferred to use different ratings extrapolated from different scales (i.e. BDI-II “anhedonia” subscale score vs. CAARMS “Depression” item 7.2 subscore).

As psychometric index of *suicide risk*, we used the BDI-II item 9 (which covers recent [2-week] suicidal ideation), both at baseline and after the 2 years of follow-up. Specifically, subjects rate their agreement with the following statements during the preceding 14 days: “I would kill myself if I had the chance” (score = 3), “I would like to kill myself” (score = 2), “I have thoughts of killing myself, but I would not carry them out” (score = 1) and “I don’t have thoughts of killing myself” (score = 0) (Beck et al., 2006). A BDI-II item 9 score of  $\geq 1$  showed a statistically relevant association with the total score of the Beck Scale for Suicidal Ideation (Taylor et al., 2015).

### 2.3. Procedures and statistical analysis

The axis-I diagnosis was made by at least two trained ReARMS team members using the Structured Clinical Interview for DSM-IV-TR axis I Disorders (SCID-I) (First et al., 2002). After CAARMS interviews, all the participants were divided into 3 groups in accordance with the

FEP/UHR criteria: (a) FEP group, UHR group (i.e. BLIPS, APS and GRFD) and (c) CAARMS- (i.e. those subjects who were under the threshold of the CAARMS FEP/UHR inclusion criteria) (Yung et al., 2005).

All the individuals entered the ReARMS program were assigned to a multi-professional team (including a clinical psychologist, a psychiatrist and a case-manager for early recovery-oriented rehabilitation), generally within 3 weeks. Based on their symptoms, UHR and FEP subjects were provided with a comprehensive 2-year intervention package combining (a) a multi-element psychosocial intervention (included individual Cognitive-Behavioral Therapy [CBT], psychoeducational sessions for family members and a recovery-oriented case management) and (b) a pharmacological treatment (in accordance with the current guidelines on the topic) (Schmidt et al., 2015; NICE, 2016). Antipsychotic medication was avoided unless UHR individuals (a) were overwhelmed by abruptly worsening, overt psychotic symptoms; (b) were rapidly deteriorating in daily functioning, (c) had an imminent risk of severe violence or suicide, or (d) did not respond to any other treatment.

Data were analyzed using the Statistical Package for Social Science (SPSS) for Windows, version 15.0 (SPSS Inc., 2010). All tests were two-tailed with statistical significance set at 0.05. At baseline, socio-demographic parameters and anhedonia scores were examined by evaluating inter-group comparisons (i.e., UHR vs. FEP vs. CAARMS-). Specifically, categorical variables were analyzed using the Chi-square test, while the Kruskal–Wallis test (with the Mann–Whitney *U* test as post-hoc procedure) was used to compare continuous parameters. The Holm–Bonferroni *p* value correction was also performed to control the problem of multiple comparisons (Holm, 1979).

As the main purpose of the current research was to investigate the relationship between anhedonia levels and suicidal thoughts over a 2-year follow-up period, we decided to follow the statistical procedure used by Winer et al. (2014a) in an interesting study examining prediction on suicidal ideation by anhedonia in a large psychiatric inpatient sample. Specifically, in order to assess whether this relationship remained significant when accounting for clinical depression severity, we performed hierarchical regressions with the BDI-II “Anhedonia” subscale score as independent parameter in the step 1, the CAARMS “Depression” item 7.2 subscore as additional independent variable in the step 2, and the BDI-II “Suicidal ideation” item 9 subscore as the dependent measure. As we hypothesized that anhedonia would have predicted suicidal ideation at entry, at termination and over time, we repeated such analysis both at baseline and across the 2 years of follow-up, individually in each group examined (i.e. UHR, FEP and CAARMS-) and within specific DSM-IV-TR diagnostic categories (i.e. schizotypal personality disorder and major depressive disorder in UHR participants; major depressive disorder with psychotic features, Schizophrenia Spectrum Disorders [SSD] and Non-Schizophrenia Spectrum Disorders [NSSD] in FEP participants). Specifically, after SCID-I administration, FEP participants with schizophrenia and

schizophreniform disorder were included in the SSD subsample on the basis that these categories have negative symptoms as part of their definition in recognized diagnostic criteria (such as the DSM-IV-TR) (APA, 2000). In contrast, the NSSD subgroup included all other diagnoses of psychosis (Pelizza et al., 2021b). In all the subgroups, we examined the associations among the above mentioned parameters (i.e. anhedonia, suicidal ideation and depression) at the initial assessment time (T0), at the 2-year assessment time (T2) and along the 2-year follow-up period (i.e. through the difference [Delta] in T0 and T2 scores) (Pelizza et al., 2021c).

### 3. Results

Over the course of this research, 338 individuals were consecutively enrolled within the ReARMS protocol. Clinical and socio-demographic variables of the total sample and the three subgroups are shown in the Table 1.

Within the UHR group ( $n = 96$ ; 28.4% of the total sample), 86 (89.6%) participants met APS criteria, 5 met BLIPS criteria and 5 met GRFD criteria. According to the DSM-IV-TR criteria (APA, 2000), UHR subjects were diagnosed with major depressive disorder ( $n = 45$ ; 46.8% of the UHR total sample), schizotypal personality disorder ( $n = 22$ ), obsessive-compulsive disorder ( $n = 12$ ), anxiety disorders ( $n = 12$ ) and brief psychotic disorder ( $n = 5$ ). Specifically, the 5 UHR individuals with brief psychotic disorder also met BLIPS criteria (i.e. they had a history of fleeting psychotic experiences that spontaneously resolved within one week, without the use of antipsychotic medication (Yung et al., 2005).

FEP patients ( $n = 146$ ; 43.2% of the total group) were diagnosed with DSM-IV-TR schizophrenia ( $n = 66$ ; 45.2% of FEP participants), psychotic disorder not otherwise specified ( $n = 31$ ), affective (major depressive or bipolar) psychosis ( $n = 27$ ), brief psychotic disorder ( $n = 14$ ) and schizoaffective disorder ( $n = 8$ ). The FEP subjects with brief psychotic disorder did not obviously meet BLIPS criteria and were outside the UHR definition (e.g. they experienced full-blown psychotic symptoms from more than one week and/or having resolved within one month and with the use of antipsychotic drugs).

Finally, CAARMS- individuals ( $n = 96$ ; 28.4% of the total group) were affected by DSM-IV-TR non-schizotypal personality disorder ( $n = 35$ ; 36.4% of the CAARMS- participants), depressive disorders ( $n = 25$ ), anxiety disorders ( $n = 24$ ), obsessive-compulsive disorder ( $n = 7$ ) and eating disorders ( $n = 5$ ).

In comparison with UHR and CAARMS-, FEP participants showed a greater percentage of males and a higher age at entry (Table 1). Moreover, UHR subjects had a younger age at the ReARMS enrollment compared to CAARMS- individuals. Finally, FEP patients showed a significantly longer Duration of Untreated Illness (DUI, defined as the time interval [in weeks] between the onset of a prominent psychiatric symptom and the administration of the first pharmacological/

**Table 1**

Demographic characteristics and baseline anhedonia levels of the total sample and the three subgroups.

Variable	Total sample ( $n = 338$ )	CAARMS- ( $n = 96$ )	UHR ( $n = 96$ )	FEP ( $n = 146$ )	$\chi^2$	Post hoc test
Gender (males)	186 (55.0%)	47 (49.0%)	43 (44.8%)	96 (65.8%)	12.3 <sup>b</sup>	FEP > UHR = CAARMS- <sup>e,f</sup>
Ethnic group (White Caucasian)	297 (87.9%)	83 (86.5%)	88 (91.7%)	126 (86.3%)	1.81	–
Mother tongue (Italian)	307 (91.1%)	90 (93.8%)	89 (93.7%)	128 (87.7%)	3.73	–
Age at entry	21.33 ± 5.84	21.07 ± 6.32	18.85 ± 4.32	23.12 ± 5.80	32.2 <sup>a</sup>	FEP > CAARMS->UHR <sup>d,e,f</sup>
Education (in years)	11.71 ± 2.44	11.64 ± 2.48	11.56 ± 2.38	11.86 ± 2.46	1.26	–
DUI (in weeks)	77.61 ± 60.78	66.51 ± 54.60	65.41 ± 48.52	94.48 ± 69.19	8.44 <sup>c</sup>	FEP > UHR <sup>f</sup>
Comorbid substance abuse	104 (30.8%)	24 (25.0%)	13 (13.5%)	67 (45.9%)	23.41 <sup>a</sup>	FEP > UHR = CAARMS- <sup>d,e</sup>
<b>Anhedonia</b>	4.12 ± 2.80	3.54 ± 2.52	4.01 ± 2.63	4.57 ± 3.02	30.55 <sup>a</sup>	FEP > CAARMS- <sup>f</sup>
BDI-II “Anhedonia” subscale (baseline)						

Frequencies (percentages), mean ± standard deviation, Kruskal–Wallis and Chi-squared test ( $\chi^2$ ) values are reported. Post-hoc analyses were performed using the Mann–Whitney *U* test. <sup>a</sup> $p < 0.001$ ; <sup>b</sup> $p < 0.01$ ; <sup>c</sup> $p < 0.05$ ; <sup>d</sup>Holm–Bonferroni corrected *p* value  $< 0.001$ ; <sup>e</sup>Holm–Bonferroni corrected *p* value  $< 0.01$ ; <sup>f</sup>Holm–Bonferroni corrected *p* value  $< 0.05$ . CAARMS = Comprehensive Assessment of At-Risk Mental States; FEP = First Episode Psychosis; UHR = participants who met CAARMS Ultra-High Risk (UHR) criteria; CAARMS- = participants who were below CAARMS-defined UHR/FEP criteria; DUI = Duration of Untreated Illness; BDI-II = Beck Depression Inventory-II Edition.

psychological treatment) (Rapp et al., 2017) in comparison with UHR participants. No inter-group differences in terms of years of education, mother tongue and ethnic group were found.

Compared to CAARMS-, FEP patients had a significantly higher BDI-II “Anhedonia” subscale score at baseline (Table 1). No difference in anhedonia levels at entry was found between FEP and UHR participants.

As of March 2019, 78 UHR individuals (81.2% of the UHR total group) completed the 2 years of follow-up, 8 dropped-out before reaching the 2-year assessment time and 6 moved out from the catchment area (i.e. it was not possible to reach them for the final psychopathological evaluation). Moreover, 122 FEP patients (83.6% of the FEP total sample) completed the 2-year follow-up period, 12 dropped-out before achieving the 2-year evaluation time (three of them died by suicide) and the remaining 12 moved out from the catchment area. Finally, 84 CAARMS- individuals (87.5% of the CAARMS- total group) completed the 2 years of follow-up, 9 dropped-out before reaching the 2-year assessment time and 6 moved out from the catchment area.

### 3.1. Relationships between anhedonia and suicidal ideation in the three subgroups

1) Within the UHR sample, hierarchical regression analyses showed significant positive associations between BDI-II “Anhedonia” subscale scores and BDI-II (“Suicidal Ideation”) item 9 subscores both at baseline and at follow-up termination, as well as between delta in T0 and T2 BDI-II “Anhedonia” subscale scores and delta in T0 and T2 BDI-II item 9 subscores (Table 2). When we added clinical depression in the step 2 of our regression analyses, both BDI-II “Anhedonia” subscale score and CAARMS “Depression” item 7.2 subscore significantly predicted BDI-II item 9 subscore at baseline. Likewise, delta in T0 and T2 BDI-II item 9 subscores was significantly predicted by both delta in T0 and T2 BDI-II “Anhedonia” subscale scores and delta in T0 and T2 CAARMS “Depression” item subscores. However, anhedonia levels had greater  $\beta$  coefficients and a higher magnitude of their effects on suicidal ideation than clinical depression in both statistically relevant regression models. Differently, the BDI-II “Anhedonia” subscale score remained associated with BDI-II item 9 subscore at termination, independent of CAARMS “Depression” item subscore.

However, exclusively considering UHR participants with DSM-IV-TR depressive disorders ( $n = 46$ ), regression analysis results revealed significant positive associations between BDI-II “Anhedonia” subscale scores and BDI-II (“Suicidal Ideation”) item 9 subscores at entry, across the 2-year follow-up period and at the end of our longitudinal observation, independent of CAARMS “Depression” item subscores (Table 3). On the contrary, no relevant associations between anhedonia and suicidal ideation were found in UHR subjects affected by DSM-IV-TR schizotypal personality disorders ( $n = 22$ ).

1) In the FEP sample, hierarchical regression analyses showed significant positive associations between BDI-II “Anhedonia” subscale scores and BDI-II (“Suicidal Ideation”) item 9 subscores both at baseline and after the 2 years of follow-up, as well as between delta in T0 and T2 BDI-II “Anhedonia” subscale scores and delta in T0 and T2 BDI-II item 9 subscores (Table 2). In all three statistically relevant regression models, anhedonia levels remained associated with suicidal ideation, independent of CAARMS “Depression” subscores.

Considering specific diagnostic categories of FEP patients, anhedonia maintained relevant associations with suicidal thoughts at entry, along the 2-year follow-up period and at the end of our longitudinal study (independent of CAARMS “Depression” item scores) in FEP participants affected by both NSSD ( $n = 72$ ) and major depressive disorder with psychotic features ( $n = 20$ ) (Table 4). On the contrary, in FEP individuals with SSD ( $n = 74$ ), a significant relationship between hedonic deficits and suicidal ideation (independent of CAARMS “Depression”

item score) was only found at baseline assessment.

1) Finally, hierarchical regression analyses in the CAARMS- subsample showed significant positive associations between BDI-II “Anhedonia” subscale scores and BDI-II (“Suicidal Ideation”) item 9 subscores both at baseline and at termination (Table 2). In both statistically significant regression models, anhedonia levels remained associated with suicidal ideation, independent of CAARMS “Depression” item subscores. No statistically significant association was found between delta in T0 and T2 BDI-II “Anhedonia” subscale scores and delta in T0 and T2 BDI-II item 9 subscores.

## 4. Discussion

As regards *baseline anhedonia* levels, although FEP participants had more severe hedonic deficits than CAARMS- subjects, no difference in terms of current (2-week) inability to feel pleasure was observed between UHR and FEP individuals. These findings suggest that (1) anhedonia in young people at UHR of psychosis is similar in severity from that of FEP subjects, already at their first help-seeking contact with specialized EIP services; and (2) a relevant impairment in the ability to be engaged in pleasant/rewarding activities may also be observed already during the early phases of psychosis. Our results are not concordant with what reported by Jhung et al. (2016), who found higher levels of current anhedonia in young patients with recent-onset schizophrenia compared to UHR peers, independent of comorbid depression.

However, our findings in anhedonia severity did not appear to be related with differences in socio-demographic and clinical features. Indeed, no relevant associations in terms of gender ( $\delta$  vs.  $\varphi = 3.94 \pm 2.80$  vs.  $4.34 \pm 2.80$ ; Mann-Whitney's  $z = -1.530$ ;  $p = 0.126$ ), age at entry (Spearman's  $\rho = -0.075$ ;  $p = 0.367$ ), years of education ( $\rho = 0.097$ ;  $p = 0.074$ ), ethnic group (Caucasian vs. Non-Caucasian =  $4.14 \pm 2.82$  vs.  $3.98 \pm 2.75$ ;  $z = -0.246$ ;  $p = 0.805$ ), mother tongue (Italian vs. Non-Italian =  $4.10 \pm 2.82$  vs.  $4.30 \pm 2.73$ ;  $z = -0.590$ ;  $p = 0.555$ ) and DUI ( $\rho = 0.059$ ;  $p = 0.364$ ) were found in the total sample.

In the FEP group, a significant, enduring relationship between anhedonia levels and suicidal ideation was found at baseline and across the 2 years of follow-up, independent of depression severity. This is in line with what observed by Winer et al. (2014a) in a large population of psychiatric inpatient sample, suggesting that the BDI-II “Anhedonia” subscale was significantly associated with suicidality cross-sectionally at baseline and at termination (i.e. after a 6-week follow-up period), and that change in hedonic deficits from baseline to termination predicted change in suicidality from baseline to termination, as well as level of suicidality at termination. Moreover, the authors reported that anhedonia remained a robust predictor of suicidal thoughts, even after accounting for cognitive/depressive symptoms of depression. Therefore, our results seem to indicate that anhedonia in FEP patients may be considered as an enduring predictive measure of suicidality up to a 2-year period after their first help-seeking contact with a specialized EIP service. Thus, a careful longitudinal monitoring on hedonic deficits in FEP patients can be helpful in preventing suicidal behaviors. Moreover, specific pharmacological and/or psychosocial interventions on anhedonia within specialized EIP program may also overtime reduce suicide risk in young people with FEP (Pelizza et al., 2020d). Specifically, this pattern of enduring associations appeared to be more typical of FEP patients with NSSD or major depression with psychotic features than of FEP subjects with SSD, who showed a relevant correlation between anhedonia and suicidal ideation (independent of depression severity) exclusively at baseline. In this respect, in a recent review about suicide and anhedonia Bonanni et al. (2019) reported a consistent association between suicidal behavior and hedonic deficits exclusively for affective disorders and post-traumatic stress disorder. Differently, the results of this review revealed inconsistencies of this relationship for schizophrenia spectrum disorders.

Differently in the UHR sample, the enduring relationship between

**Table 2**

Hierarchical regression of suicidal ideation by anhedonia levels and clinical depression severity across the 2-year follow-up period in the three subgroups.

UHR (n = 96)	B	SE	95% CI for B		β	p	R <sup>2</sup> = 0.114
			Lower	Upper			
<b>Baseline BDI-II item 9</b>							
Step 1	0.245	0.126	-0.005	0.495	-	0.055	R <sup>2</sup> = 0.158
Constant	0.110	0.026	0.058	0.163	0.397	<b>0.000</b>	F = 17.60
BDI-II "Anhedonia" subscale score	-0.122	0.211	-0.541	0.296	-	0.563	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.098	0.027	0.045	0.150	0.351	<b>0.000</b>	R <sup>2</sup> = 0.198
BDI-II "Anhedonia" subscale score	0.116	0.054	0.009	0.223	0.205	<b>0.034</b>	F = 11.45
CAARMS "Depression" item 7.2 subscore							<b>p = 0.000</b>
<b>TOT2 Delta BDI-II item 9</b>							
Step 1	0.185	0.106	-0.029	0.398	-	0.088	R <sup>2</sup> = 0.421
Constant	0.160	0.030	0.099	0.222	0.649	<b>0.000</b>	F = 27.66
TOT2 Delta BDI-II "Anhedonia" subscale score	0.010	0.128	-0.249	0.269	-	0.939	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.149	0.029	0.089	0.208	0.601	<b>0.000</b>	R <sup>2</sup> = 0.489
TOT2 Delta BDI-II "Anhedonia" subscale score	0.122	0.055	0.011	0.234	0.265	<b>0.033</b>	F = 17.72
TOT2 Delta CAARMS "Depression" item 7.2 subscore							<b>p = 0.000</b>
<b>T2 BDI-II item 9</b>							
Step 1	0.021	0.107	-0.196	0.237	-	0.846	R <sup>2</sup> = 0.203
Constant	0.096	0.031	0.034	0.159	0.451	<b>0.003</b>	F = 9.70
T2 BDI-II "Anhedonia" subscale score	0.064	0.126	-0.190	0.319	-	0.611	<b>p = 0.003</b>
<b>Step 2</b>							
Constant	0.108	0.036	0.036	0.181	0.506	<b>0.004</b>	R <sup>2</sup> = 0.213
T2 BDI-II "Anhedonia" subscale score	-0.039	0.058	-0.155	0.078	-0.112	0.506	F = 5.01
T2 CAARMS "Depression" item 7.2 subscore							<b>p = 0.012</b>
<b>FEP (n = 146)</b>							
<b>Baseline BDI-II item 9</b>							
Step 1	0.048	0.093	-0.136	0.232	-	0.607	R <sup>2</sup> = 0.199
Constant	0.102	0.01	0.068	0.135	0.446	<b>0.000</b>	F = 35.60
BDI-II "Anhedonia" subscale score	-0.042	0.126	-0.291	0.208	-	0.742	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.095	0.018	0.059	0.131	0.417	<b>0.000</b>	R <sup>2</sup> = 0.205
BDI-II "Anhedonia" subscale score	0.036	0.034	-0.031	0.103	0.084	0.295	F = 18.36
CAARMS "Depression" item 7.2 subscore							<b>p = 0.000</b>
<b>TOT2 Delta BDI-II item 9</b>							
Step 1	-0.014	0.099	-0.212	0.184	-	0.888	R <sup>2</sup> = 0.241
Constant	0.099	0.024	0.050	0.147	0.490	<b>0.000</b>	F = 16.78
TOT2 Delta BDI-II "Anhedonia" subscale score	-0.021	0.103	-0.228	0.186	-	0.839	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.096	0.027	0.042	0.150	0.476	<b>0.001</b>	R <sup>2</sup> = 0.242
TOT2 Delta BDI-II "Anhedonia" subscale score	0.011	0.043	-0.076	0.099	0.035	0.795	F = 8.28
TOT2 Delta CAARMS "Depression" item 7.2 subscore							<b>p = 0.001</b>
<b>T2 BDI-II item 9</b>							
Step 1	-0.150	0.074	-0.299	-0.002	-	0.047	R <sup>2</sup> = 0.581
Constant	0.170	0.020	0.130	0.210	0.762	<b>0.000</b>	F = 73.41
T2 BDI-II "Anhedonia" subscale score	-0.206	0.084	-0.375	-0.038	-	0.018	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.144	0.027	0.089	0.199	0.645	<b>0.000</b>	R <sup>2</sup> = 0.595
T2 BDI-II "Anhedonia" subscale score	0.066	0.049	-0.032	0.164	0.168	0.180	F = 38.21
T2 CAARMS "Depression" item 7.2 subscore							<b>p = 0.000</b>
<b>CAARMS (n = 96)</b>							
<b>Baseline BDI-II item 9</b>							
Step 1	0.048	0.113	-0.176	0.273	-	0.670	R <sup>2</sup> = 0.152
Constant	0.107	0.026	0.055	0.159	0.390	<b>0.000</b>	F = 16.89
BDI-II "Anhedonia" subscale score	-0.031	0.140	-0.308	0.246	-	0.826	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.093	0.030	0.034	0.152	0.339	<b>0.002</b>	R <sup>2</sup> = 0.161
BDI-II "Anhedonia" subscale score	0.049	0.050	-0.051	0.149	0.105	0.337	F = 8.91
CAARMS "Depression" item 7.2 subscore							<b>p = 0.000</b>
<b>TOT2 Delta BDI-II item 9</b>							
Step 1	-0.104	0.193	-0.506	0.297	-	0.595	R <sup>2</sup> = 0.153
Constant	0.093	0.047	-0.004	0.189	0.391	0.059	F = 3.97
TOT2 Delta BDI-II "Anhedonia" subscale score	-0.103	0.197	-0.513	0.306	-	0.606	<b>p = 0.059</b>
<b>Step 2</b>							
Constant	0.075	0.061	-0.052	0.202	0.317	0.231	R <sup>2</sup> = 0.161
TOT2 Delta BDI-II "Anhedonia" subscale score	0.037	0.080	-0.130	0.203	0.117	0.654	F = 2.02
TOT2 Delta CAARMS "Depression" item 7.2 subscore							<b>p = 0.158</b>
<b>T2 BDI-II item 9</b>							
Step 1	-0.084	0.099	-0.289	0.122	-	0.408	R <sup>2</sup> = 0.419
Constant	0.231	0.058	0.111	0.351	0.647	<b>0.001</b>	F = 15.85

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**Table 2 (continued)**

CAARMS-(n = 96)	B	SE	95% CI for B		$\beta$	p	R <sup>2</sup> = 0.114
			Lower	Upper			
T2 BDI-II "Anhedonia" subscale score	-0.052	0.103	-0.266	0.161	-	0.615	<b>p = 0.001</b>
Step 2	0.327	0.104	0.110	0.544	0.916	<b>0.005</b>	R <sup>2</sup> = 0.451
Constant	-0.130	0.117	-0.374	0.115	-0.322	0.282	F = 8.61
T2 BDI-II "Anhedonia" subscale score							<b>p = 0.002</b>
T2 CAARMS "Depression" item 7.2 subscore							

BDI-II = Beck Depression Inventory; CAARMS = Comprehensive Assessment of At-Risk Mental States; UHR = Ultra High Risk; FEP = First Episode Psychosis; CAARMS- = individuals who were below the CAARMS FEP/UHR criteria; T0 = baseline assessment time; T2 = 2-year assessment time; Delta = difference in T0 and T2 scores. B = regression coefficient, SE = standard error, 95% CI = 95% Confident Intervals for B,  $\beta$  = standardized regression coefficient; p = statistical significance, R<sup>2</sup> = coefficient of determination; F = F test value. Statistically significant p values are in bold.

**Table 3**

Hierarchical regression of suicidal ideation by anhedonia levels and clinical depression severity across the 2-year follow-up period in specific UHR subgroups.

UHR with Schizotypal Personality Disorder (n = 22)	B	SE	95% CI for B		$\beta$	p	R <sup>2</sup> = 0.114
			Lower	Upper			
Baseline BDI-II item 9							
Step 1	0.216	0.175	-0.149	0.582	-	0.231	R <sup>2</sup> = 0.025
Constant	0.029	0.040	-0.055	0.112	0.159	0.481	F = 0.52
BDI-II "Anhedonia" subscale score	-0.087	0.271	-0.654	0.480	-	0.751	p = 0.481
Step 2	0.021	0.039	-0.061	0.103	0.116	0.599	R <sup>2</sup> = 0.121
Constant	0.104	0.072	-0.047	0.255	0.313	0.165	F = 1.31
BDI-II "Anhedonia" subscale score							p = 0.292
CAARMS "Depression" item 7.2 subscore							
TOT2 Delta BDI-II item 9							
Step 1	0.310	0.172	-0.086	0.706	-	0.109	R <sup>2</sup> = 0.004
Constant	-0.011	0.064	-0.160	0.138	-0.061	0.867	F = 0.03
TOT2 Delta BDI-II "Anhedonia" subscale score	0.097	0.251	-0.497	0.691	-	0.711	p = 0.867
Step 2	-0.016	0.063	-0.166	0.134	-0.089	0.804	R <sup>2</sup> = 0.161
Constant	0.109	0.095	-0.116	0.334	0.398	0.290	F = 0.67
TOT2 Delta BDI-II "Anhedonia" subscale score							p = 0.541
TOT2 Delta CAARMS "Depression" item 7.2 subscore							
T2 BDI-II item 9							
Step 1	0.065	0.172	-0.322	0.461	-	0.717	R <sup>2</sup> = 0.153
Constant	0.065	0.054	-0.059	0.188	0.391	0.263	F = 1.45
T2 BDI-II "Anhedonia" subscale score	-0.050	0.179	-0.473	0.374	-	0.789	p = 0.263
Step 2	0.010	0.062	-0.137	0.158	0.062	0.874	R <sup>2</sup> = 0.350
Constant	0.163	0.112	-0.101	0.427	0.553	0.188	F = 1.89
T2 BDI-II "Anhedonia" subscale score							p = 0.221
T2 CAARMS "Depression" item 7.2 subscore							
UHR with Depressive Disorders (n = 45)							R <sup>2</sup> = 0.114
Baseline BDI-II item 9							
Step 1	0.297	0.218	-0.142	0.736	-	0.180	R <sup>2</sup> = 0.171
Constant	0.136	0.046	0.044	0.228	0.414	<b>0.005</b>	F = 8.89
BDI-II "Anhedonia" subscale score	0.095	0.374	-0.659	0.849	-	0.801	<b>p = 0.005</b>
Step 2	0.129	0.047	0.033	0.224	0.391	<b>0.010</b>	R <sup>2</sup> = 0.180
Constant	0.062	0.092	-0.124	0.248	0.096	0.508	F = 4.61
BDI-II "Anhedonia" subscale score							<b>p = 0.015</b>
CAARMS "Depression" item 7.2 subscore							
TOT2 Delta BDI-II item 9							
Step 1	0.097	0.179	-0.288	0.481	-	0.598	R <sup>2</sup> = 0.580
Constant	0.218	0.050	0.112	0.324	0.762	<b>0.001</b>	F = 19.33
TOT2 Delta BDI-II "Anhedonia" subscale score	-0.074	0.202	-0.509	0.362	-	0.721	<b>p = 0.001</b>
Step 2	0.185	0.052	0.074	0.296	0.646	<b>0.003</b>	R <sup>2</sup> = 0.648
Constant	0.169	0.107	-0.062	0.400	0.285	0.138	F = 4.51
TOT2 Delta BDI-II "Anhedonia" subscale score							<b>p = 0.001</b>
TOT2 Delta CAARMS "Depression" item 7.2 subscore							
T2 BDI-II item 9							
Step 1	-0.324	0.162	-0.672	0.024	-	0.066	R <sup>2</sup> = 0.691
Constant	0.273	0.049	0.168	0.377	0.831	<b>0.000</b>	F = 31.28
T2 BDI-II "Anhedonia" subscale score	-0.210	0.180	-0.599	0.179	-	0.265	<b>p = 0.000</b>
Step 2	0.297	0.051	0.187	0.407	0.904	<b>0.000</b>	R <sup>2</sup> = 0.728
Constant	-0.083	0.062	-0.217	0.052	-0.205	0.208	F = 17.36
T2 BDI-II "Anhedonia" subscale score							<b>p = 0.000</b>
T2 CAARMS "Depression" item 7.2 subscore							

BDI-II = Beck Depression Inventory; CAARMS = Comprehensive Assessment of At-Risk Mental States; UHR = Ultra High Risk; T0 = baseline assessment time; T2 = 2-year assessment time; Delta = difference in T0 and T2 scores. B = regression coefficient, SE = standard error, 95% CI = 95% Confident Intervals for B,  $\beta$  = standardized regression coefficient; p = statistical significance, R<sup>2</sup> = coefficient of determination; F = F test value. Statistically significant p values are in bold.

**Table 4**

Hierarchical regression of suicidal ideation by anhedonia levels and clinical depression severity across the 2-year follow-up period in specific FEP subgroups.

FEP with Schizophrenia Spectrum Disorders (n = 74)	B	SE	95% CI for B		$\beta$	p	R <sup>2</sup> = 0.114
			Lower	Upper			
<b>Baseline BDI-II item 9</b>							
Step 1	0.085	0.137	-0.188	0.358	-	0.537	R <sup>2</sup> = 0.159
Constant	0.094	0.026	0.043	0.145	0.399	<b>0.000</b>	F = 13.44
BDI-II "Anhedonia" subscale score	-0.033	0.188	-0.407	0.341	-	0.862	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.079	0.030	0.020	0.139	0.338	<b>0.010</b>	R <sup>2</sup> = 0.169
BDI-II "Anhedonia" subscale score	0.052	0.056	-0.060	0.164	0.117	0.360	F = 7.13
CAARMS "Depression" item 7.2 subscore							<b>p = 0.002</b>
<b>T0T2 Delta BDI-II item 9</b>							
Step 1	0.164	0.113	-0.070	0.398	-	0.161	R <sup>2</sup> = 0.157
Constant	0.050	0.027	0.001	0.117	0.320	0.051	F = 3.94
T0T2 Delta BDI-II "Anhedonia" subscale score	0.174	0.132	-0.101	0.449	-	0.203	p = 0.051
<b>Step 2</b>							
Constant	0.062	0.030	-0.001	0.125	0.434	0.052	R <sup>2</sup> = 0.178
T0T2 Delta BDI-II "Anhedonia" subscale score	-0.009	0.055	-0.122	0.105	-0.033	0.877	F = 2.37
T0T2 Delta CAARMS "Depression" item 7.2 subscore							<b>p = 0.116</b>
<b>T2 BDI-II item 9</b>							
Step 1	0.052	0.054	-0.060	0.165	-	0.347	R <sup>2</sup> = 0.005
Constant	-0.007	0.022	-0.053	0.038	-0.071	0.738	F = 0.11
T2 BDI-II "Anhedonia" subscale score	0.087	0.065	-0.047	0.221	-	0.191	p = 0.738
<b>Step 2</b>							
Constant	-0.001	0.023	-0.048	0.047	-0.005	0.980	R <sup>2</sup> = 0.049
T2 BDI-II "Anhedonia" subscale score	-0.035	0.035	-0.107	0.037	-0.219	0.327	F = 0.56
T2 CAARMS "Depression" item 7.2 subscore							<b>p = 0.579</b>
<b>FEP with non-Schizophrenia Spectrum Disorders (n = 72)</b>							
	B	SE	95% CI for B		B	p	R <sup>2</sup> = 0.114
			Lower	Upper			
<b>Baseline BDI-II item 9</b>							
Step 1	0.014	0.128	-0.241	0.269	-	0.913	R <sup>2</sup> = 0.242
Constant	0.109	0.023	0.063	0.155	0.492	<b>0.000</b>	F = 22.35
BDI-II "Anhedonia" subscale score	-0.071	0.175	-0.421	0.278	-	0.686	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.106	0.024	0.058	0.153	0.476	<b>0.000</b>	R <sup>2</sup> = 0.226
BDI-II "Anhedonia" subscale score	0.032	0.044	-0.057	0.120	0.076	0.478	F = 11.35
CAARMS "Depression" item 7.2 subscore							<b>p = 0.000</b>
<b>T0T2 Delta BDI-II item 9</b>							
Step 1	-0.207	0.153	-0.521	0.108	-	0.189	R <sup>2</sup> = 0.336
Constant	0.144	0.038	0.065	0.222	0.580	<b>0.001</b>	F = 14.17
T0T2 Delta BDI-II "Anhedonia" subscale score	-0.206	0.156	-0.527	0.115	-	0.198	<b>p = 0.001</b>
<b>Step 2</b>							
Constant	0.145	0.044	0.055	0.235	0.584	<b>0.003</b>	R <sup>2</sup> = 0.336
T0T2 Delta BDI-II "Anhedonia" subscale score	-0.004	0.067	-0.140	0.133	-0.010	0.957	F = 6.83
T0T2 Delta CAARMS "Depression" item 7.2 subscore							<b>p = 0.004</b>
<b>T2 BDI-II item 9</b>							
Step 1	-0.184	0.103	-0.395	0.026	-	0.084	R <sup>2</sup> = 0.744
Constant	0.206	0.023	0.159	0.253	0.863	<b>0.000</b>	F = 81.44
T2 BDI-II "Anhedonia" subscale score	-0.235	0.122	-0.485	0.014	-	0.064	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.181	0.038	0.102	0.260	0.760	<b>0.000</b>	R <sup>2</sup> = 0.750
T2 BDI-II "Anhedonia" subscale score	0.058	0.072	-0.091	0.206	0.129	0.432	F = 40.52
T2 CAARMS "Depression" item 7.2 subscore							<b>p = 0.000</b>
<b>FEP with Major Depressive Disorder with psychotic features (n = 20)</b>							
	B	SE	95% CI for B		$\beta$	p	R <sup>2</sup> = 0.114
			Lower	Upper			
<b>Baseline BDI-II item 9</b>							
Step 1	0.048	0.093	-0.136	0.232	-	0.607	R <sup>2</sup> = 0.199
Constant	0.102	0.017	0.068	0.135	0.446	<b>0.000</b>	F = 35.60
BDI-II "Anhedonia" subscale score	-0.042	0.126	-0.291	0.208	-	0.742	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.095	0.018	0.059	0.131	0.417	<b>0.000</b>	R <sup>2</sup> = 0.205
BDI-II "Anhedonia" subscale score	0.036	0.034	-0.031	0.103	0.084	0.295	F = 18.36
CAARMS "Depression" item 7.2 subscore							<b>p = 0.000</b>
<b>T0T2 Delta BDI-II item 9</b>							
Step 1	-0.014	0.099	-0.212	0.184	-	0.888	R <sup>2</sup> = 0.241
Constant	0.099	0.024	0.050	0.147	0.490	<b>0.000</b>	F = 316.78
T0T2 Delta BDI-II "Anhedonia" subscale score	-0.021	0.103	-0.228	0.186	-	0.839	<b>p = 0.000</b>
<b>Step 2</b>							
Constant	0.096	0.027	0.042	0.150	0.476	<b>0.001</b>	R <sup>2</sup> = 0.242
T0T2 Delta BDI-II "Anhedonia" subscale score	0.011	0.043	-0.076	0.099	0.035	0.795	F = 8.28
T0T2 Delta CAARMS "Depression" item 7.2 subscore							<b>p = 0.001</b>
<b>T2 BDI-II item 9</b>							
Step 1	-0.150	0.074	-0.299	-0.002	-	0.047	R <sup>2</sup> = 0.581
Constant	0.170	0.020	0.130	0.210	0.762	<b>0.000</b>	F = 73.41

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Table 4 (continued)

FEP with Major Depressive Disorder with psychotic features ( <i>n</i> = 20)	B	SE	95% CI for B		$\beta$	<i>p</i>	$R^2 = 0.114$
			Lower	Upper			
T2 BDI-II "Anhedonia" subscale score	-0.206	0.084	-0.375	-0.038	-	0.018	<b><i>p</i> = 0.000</b>
Step 2	0.144	0.027	0.089	0.199	0.645	<b>0.000</b>	$R^2 = 0.595$
Constant	0.066	0.049	-0.032	0.164	0.168	0.180	$F = 38.21$
T2 BDI-II "Anhedonia" subscale score							<b><i>p</i> = 0.000</b>
T2 CAARMS "Depression" item 7.2 subscore							

BDI-II = Beck Depression Inventory; CAARMS = Comprehensive Assessment of At-Risk Mental States; FEP = First Episode Psychosis; T0 = baseline assessment time; T2 = 2-year assessment time; Delta = difference in T0 and T2 scores. *B* = regression coefficient, *SE* = standard error, 95% CI = 95% Confident Intervals for *B*,  $\beta$  = standardized regression coefficient; *p* = statistical significance,  $R^2$  = coefficient of determination;  $F$  =  $F$  test value. Statistically significant *p* values are in bold.

anhedonia and suicidal thoughts across the 2 years of follow-up are not completely independent of depression severity (although hedonic deficits had a higher magnitude of effect on suicidal ideation than depressive symptoms in our hierarchical regression models). This is in line with what observed in previous studies on anhedonia in UHR populations (Gruber et al., 2018; Pelizza et al., 2020e), reporting a significant association of baseline inability to feel pleasure with comorbid depression. In addition, our findings suggest an enduring, potentiating predictive effect on suicidal thoughts by both hedonic deficits and depressive symptoms in young people at UHR of psychosis. In interpreting these results, it is necessary to take into account the high prevalence of comorbid depressive disorders commonly observed in UHR populations (Fusar-Poli et al., 2014; Poletti et al., 2019). However, exclusively considering UHR participants with DSM-IV-TR depressive disorders, the enduring associations between anhedonia and suicidal thoughts appeared to be independent of depression severity. Overall, according to Radua et al. (2018), UHR individuals with anhedonic characteristics may be not only at risk of psychosis, but also at risk of suicide. Therefore, also in UHR subjects, a longitudinal monitoring on anhedonia levels (together with symptoms of depression) can be useful in suicide prevention (Silverman et al., 2007).

Finally, within the CAARMS- group, the relationship between hedonic deficits and suicidal ideation across the 2 years of follow-up seems to less enduring, but independent of clinical depression. Specifically, it seems to involve their measures at baseline and at termination, but it is less clearly defined along the 2-year follow-up period.

#### 4.1. Limitations

Some limitations of this research should be also acknowledged. First, differences in associations between anhedonia and depression might be psychometrically influenced by the fact that BDI-II "Anhedonia" subscale score is more stable, being computed as a sum of 4 items. Differently, CAARMS "Depression" item 7.2 is just a single question, with a more unstable subscore. This potential statistical artifact must be taken into consideration when interpreting our results and it still remains a point of criticism.

Second, the lack of significant association between anhedonia and depression could be due to the difference of rater-assessment scales (CAARMS) from subjective self-reports (BDI-II). Therefore, further studies using more uniform psychometric instruments are needed. As previously mentioned, in this research we decided to use CAARMS item 7.2 to assess clinical depression (instead of the BDI-II) in order to avoid a psychometric overlapping between measures on anhedonia and depressive symptoms.

Third, our participants were not all antipsychotic-free. Antipsychotic medication (or other psychotropic drugs, such as serotonin selective reuptake inhibitors) may have indirect or direct pharmacological effects on biological mechanisms underlying hedonic response, and can create a normalizing effect in individuals who are stably treated for many weeks (Gruber et al., 2018). However, in the current research no significant correlation between anhedonia levels and equivalent dose of chlorpromazine at baseline was found in the total sample ( $\rho = 0.055$ ;  $p = 0.312$ ).

Fourth, in the present study anhedonia was assessed using a subscale combining 4 different BDI-II items. However, this self-reported instrument was not developed as stand-alone measures. Therefore, it could lack reliability and provide a limited coverage of anhedonic features (e.g., physical anhedonia aspects). Thus, further research would benefit from the use of specific, validated measures of anhedonia, such as the Snaith-Hamilton Pleasure Scale (Snaith et al., 1995), the Specific Loss of Interest and Pleasure Scale (SLIPS) (Winer et al., 2014b) or the Dimensional Anhedonia Rating Scale (DARS) (Rizvi et al., 2015).

Fifth, since the BDI-II devised to be intrinsically coherent, this could negatively affect the findings that a combination of some items of the scale (i.e., the BDI-II "Anhedonia" subscale) was statistically related to the scores on another item of the same instrument (i.e., the BDI-II item 9). Moreover, reliance upon a single self-reported measure for suicidal ideation could also be limiting the validity and generalizability of our results. Therefore, future studies investigating the association between these different constructs using independent scales (hopefully with different methods of scoring to avoid an excessive influence of the response style) are needed.

Another weakness of this research is related to our focus on general anhedonia, instead of social anhedonia, which more often showed higher severity levels in schizophrenia and in major depressive disorder than physical anhedonia (Barkus and Badcock, 2019). Thus, future studies specifically examining social anhedonia in early psychosis to replicate our findings are needed. In this respect, the Revised Social Anhedonia Scale (RSAS) (Eckblad et al., 1982) or the Anticipatory and Consummatory Interpersonal Pleasure Scale (Gooding and Pflum, 2014) may be used.

Finally, in interpreting our findings obtained in specific diagnostic categories (i.e. UHR participants with schizotypal personality disorder or DSM-IV-TR depressive disorders; FEP participants affected by major depressive disorder with psychotic features), it is necessary to take into account their small sample size. Therefore, further studies on larger diagnostic populations to confirm our promising results are needed.

#### 4.2. Conclusions

Our findings suggest to pay particular clinical attention on anhedonia in early detection and intervention in psychosis. Specifically, it seems to be relevant in predicting suicidal ideation and in preventing suicide (independent of depression) over a prolonged illness course, both in FEP and in UHR populations. Furthermore, specific pharmacological and/or psychosocial interventions on anhedonia within specialized EIP program could reduce suicide risk overtime.

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## CRedit authorship contribution statement

**Michele Poletti:** Writing – original draft, Writing – review & editing. **Lorenzo Pelizza:** Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Gwenole Loas:** Conceptualization, Writing – original draft, Writing – review & editing. **Silvia Azzali:** Data curation, Writing – review & editing. **Federica Paterlini:** Data curation, Writing – review & editing. **Sara Garlassi:** Data curation, Writing – review & editing. **Ilaria Scazza:** Data curation, Writing – review & editing. **Luigi Rocco Chiri:** Data curation, Writing – review & editing. **Simona Pupo:** Writing – review & editing. **Andrea Raballo:** Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing.

## Declaration of Competing Interest

None declared.

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